

Most Parents Favor HPV Vaccine at Younger Ages

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NEWPORT BEACH, CALIF. — A study of 61 parents of infants and children up to 10 years of age suggests that parents may favor the idea of giving the human papillomavirus vaccine at a very young age rather than during adolescence. The study also found that parents with higher socioeconomic status and education levels were more likely to reject hu-

man papillomavirus (HPV) immunization for their children at any age, a finding that could help target educational efforts for the HPV vaccine toward those demographics, Dr. Ellen S. Rome said at the annual meeting of the North American Society for Pediatric and Adolescent Gynecology. One HPV vaccine, Gardasil, is approved for use in females aged 9-26 years, and another is being considered for approval by the Food and Drug Administration.

Dr. Rome is on the speakers bureau of Merck & Co., which markets Gardasil. Studies on the use of HPV vaccine in infants and children would need to be conducted for that to happen, added Dr. Rome, head of adolescent medicine at the Cleveland Clinic. She presented the current study on behalf of the lead investigator, Dr. Laura Gillespie, also of the Cleveland Clinic, and her associates. Parents recruited from the clinic’s main campus, emergency department, and re-

gional satellite offices answered a questionnaire about demographics, attitudes about immunization, knowledge about HPV, and willingness to have their children vaccinated against HPV. The parents then were given a one-page educational sheet from the Centers for Disease Control about HPV; after reading it, they completed a second questionnaire. Before the intervention (the educational sheet), 25 parents said they wanted their children to get the HPV vaccine, 6 did not, and 30 were undecided. The higher the socioeconomic status—either income or educational level—of the parents, the less likely they were to want their children to get the HPV vaccine.

“Low-income families may have more realistic fears about what a sexually transmitted disease or HPV could mean for their child,” Dr. Rome speculated.

None of the parents who initially were for or against the vaccine changed their minds after reading the educational sheet. Among the 30 undecided parents, 12 favored vaccination after they read the sheet, 15 opposed it, and 3 did not answer the question about whether they would accept the HPV vaccine if it was offered for their child.

Beliefs that the HPV vaccine is safe and effective were significantly associated with acceptance after the intervention. Parents with higher education or income may require more aggressive education from clinicians about the vaccine’s safety and efficacy, the investigators suggested.

Among the 37 parents who approved of the HPV vaccine after the intervention, 29 (78%) said they’d prefer that it be given to young children or infants instead of to teenagers.

“They wanted to make it a baby shot,” Dr. Rome said.

The reason for that echoes findings from two previous studies of HPV vaccine acceptance by parents of children aged 10 years or older. “Parents still think that this shot is a license to have sex” if it is given to adolescents, Dr. Rome said. “That’s a myth that we’re still continuing to try to work towards busting.”

Parents with more boys in their homes were more favorable toward the HPV vaccine, “giving us hope that when the shot is available for boys,” parents will approve, she said. Merck is pursuing approval for the vaccine in boys.

Since the completion of the study, the investigators began a separate study looking at current vaccination rates within their institution, for quality improvement purposes. They’re finding near-100% acceptance of the HPV vaccine by physicians and parents in the clinic’s urban offices, but the regional satellite offices have higher rates of “late adopters” who are resistant to use of the vaccine or who reserve it for older adolescents, she said.

“The more yuppified the practice, the higher the rates of late adopters among physicians and parents,” she said. “I don’t think we have the baby shot anywhere on the horizon for the near future, so there is definitely time to work towards helping them move away from being late adopters.”

RotaTeq® [Rotavirus Vaccine, Live, Oral, Pentavalent]

BRIEF SUMMARY OF PRESCRIBING INFORMATION CONTRAINDICATIONS

A demonstrated history of hypersensitivity to any component of the vaccine. Infants who develop symptoms suggestive of hypersensitivity after receiving a dose of RotaTeq should not receive further doses of RotaTeq.

WARNINGS AND PRECAUTIONS

Immunocompromised Populations: No safety or efficacy data are available for the administration of RotaTeq to infants who are potentially immunocompromised including: Infants with blood dyscrasias, leukemia, lymphomas of any type, or other malignant neoplasms affecting the bone marrow or lymphatic system; Infants on immunosuppressive therapy (including high-dose systemic corticosteroids). RotaTeq may be administered to infants who are being treated with topical corticosteroids or inhaled steroids; Infants with primary and acquired immunodeficiency states, including HIV/AIDS or other clinical manifestations of infection with human immunodeficiency viruses; cellular immune deficiencies; and hypogammaglobulinemic and dysgammaglobulinemic states. There are insufficient data from the clinical trials to support administration of RotaTeq to infants with indeterminate HIV status who are born to mothers with HIV/AIDS; Infants who have received a blood transfusion or blood products, including immunoglobulins within 42 days. No data are available regarding potential vaccine virus transmission from vaccine recipient to nonvaccinated household or other contacts [see Shedding and Transmission].

Gastrointestinal Illness: No safety or efficacy data are available for administration of RotaTeq to infants with a history of gastrointestinal disorders including infants with active acute gastrointestinal illness, infants with chronic diarrhea and failure to thrive, and infants with a history of congenital abdominal disorders, abdominal surgery, and intussusception. Caution is advised when considering administration of RotaTeq to these infants.

Intussusception: Following administration of a previously licensed live rhesus rotavirus-based vaccine, an increased risk of intussusception was observed. In REST* (n=69,625), the data did not show an increased risk of intussusception for RotaTeq when compared to placebo. In post-marketing experience, cases of intussusception have been reported in temporal association with RotaTeq. See ADVERSE REACTIONS, Clinical Studies Experience and Post-Marketing Experience.

Shedding and Transmission: Shedding was evaluated among a subset of subjects in REST 4 to 6 days after each dose and among all subjects who submitted a stool antigen rotavirus positive sample at any time. RotaTeq was shed in the stools of 32 of 360 [8.9%, 95% CI (6.2%, 12.3%)] vaccine recipients tested after dose 1; 0 of 249 [0.0%, 95% CI (0.0%, 1.5%)] vaccine recipients tested after dose 2; and in 1 of 385 [0.3%, 95% CI (<0.1%, 1.4%)] vaccine recipients after dose 3. In phase 3 studies, shedding was observed as early as 1 day and as late as 15 days after a dose. Transmission was not evaluated. Caution is advised when considering whether to administer RotaTeq to individuals with immunodeficient close contacts such as: Individuals with malignancies or who are otherwise immunocompromised; or Individuals receiving immunosuppressive therapy. RotaTeq is a solution of live reassortant rotaviruses and can potentially be transmitted to persons who have contact with the vaccine. The potential risk of transmission of vaccine virus should be weighed against the risk of acquiring and transmitting natural rotavirus.

Febrile Illness: Febrile illness may be reason for delaying use of RotaTeq except when, in the opinion of the physician, withholding the vaccine entails a greater risk. Low-grade fever (<100.5°F [38.1°C]) itself and mild upper respiratory infection do not preclude vaccination with RotaTeq.

Incomplete Regimen: The clinical studies were not designed to assess the level of protection provided by only one or two doses of RotaTeq.

Limitations of Vaccine Effectiveness: RotaTeq may not protect all vaccine recipients against rotavirus. **Post-Exposure Prophylaxis:** No clinical data are available for RotaTeq when administered after exposure to rotavirus.

ADVERSE REACTIONS

Clinical Studies Experience: 71,725 infants were evaluated in 3 placebo-controlled clinical trials including 36,165 infants in the group that received RotaTeq and 35,560 infants in the group that received placebo. Parents/guardians were contacted on days 7, 14, and 42 after each dose regarding intussusception and any other serious adverse events. The racial distribution was as follows: White (69% in both groups); Hispanic-American (14% in both groups); Black (8% in both groups); Multiracial (5% in both groups); Asian (2% in both groups); Native American (RotaTeq 2%, placebo 1%), and Other (<1% in both groups). The gender distribution was 51% male and 49% female in both vaccination groups. Because clinical trials are conducted under conditions that may not be typical of those observed in clinical practice, the adverse reaction rates presented below may not be reflective of those observed in clinical practice.

Serious Adverse Events: Serious adverse events occurred in 2.4% of recipients of RotaTeq when compared to 2.6% of placebo recipients within the 42-day period of a dose in the phase 3 clinical studies of RotaTeq. The most frequently reported serious adverse events for RotaTeq compared to placebo were: bronchiolitis (0.6% RotaTeq vs. 0.7% Placebo), gastroenteritis (0.2% RotaTeq vs. 0.3% Placebo), pneumonia (0.2% RotaTeq vs. 0.2% Placebo), fever (0.1% RotaTeq vs. 0.1% Placebo), and urinary tract infection (0.1% RotaTeq vs. 0.1% Placebo).

Deaths: Across the clinical studies, 52 deaths were reported. There were 25 deaths in the RotaTeq recipients compared to 27 deaths in the placebo recipients. The most commonly reported cause of death was sudden infant death syndrome, which was observed in 8 recipients of RotaTeq and 9 placebo recipients.

Intussusception: In REST, 34,837 vaccine recipients and 34,788 placebo recipients were monitored by active surveillance to identify potential cases of intussusception at 7, 14, and 42 days after each dose, and every 6 weeks thereafter for 1 year after the first dose. For the primary safety outcome, cases of intussusception occurring within 42 days of any dose, there were 6 cases among RotaTeq recipients and 5 cases among placebo recipients (see Table 1). The data did not suggest an increased risk of intussusception relative to placebo.

Table 1 Confirmed cases of intussusception in recipients of RotaTeq as compared with placebo recipients during REST		
	RotaTeq (n=34,837)	Placebo (n=34,788)
Confirmed intussusception cases within 42 days of any dose	6	5
Relative risk (95% CI) [†]		1.6 (0.4, 6.4)
Confirmed intussusception cases within 365 days of dose 1	13	15
Relative risk (95% CI)		0.9 (0.4, 1.9)

[†]Relative risk and 95% confidence interval based upon group sequential design stopping criteria employed in REST.

Among vaccine recipients, there were no confirmed cases of intussusception within the 42-day period after the first dose, which was the period of highest risk for the rhesus rotavirus-based product (see Table 2).

Table 2 Intussusception cases by day range in relation to dose in REST								
	Dose 1		Dose 2		Dose 3		Any Dose	
Day Range	RotaTeq	Placebo	RotaTeq	Placebo	RotaTeq	Placebo	RotaTeq	Placebo
1-7	0	0	1	0	0	0	1	0
1-14	0	0	1	0	0	1	1	1
1-21	0	0	3	0	0	1	3	1
1-42	0	1	4	1	2	3	6	5

All of the children who developed intussusception recovered without sequelae with the exception of a 9-month-old male who developed intussusception 98 days after dose 3 and died of post-operative sepsis. There was a single case of intussusception among 2,470 recipients of RotaTeq in a 7-month-old male in the phase 1 and 2 studies (716 placebo recipients).

[†]Rotavirus Efficacy and Safety Trial

Hematochezia: Hematochezia reported as an adverse experience occurred in 0.6% (39/6,130) of vaccine and 0.6% (34/5,560) of placebo recipients within 42 days of any dose. Hematochezia reported as a serious adverse experience occurred in <0.1% (4/36,150) of vaccine and <0.1% (7/35,536) of placebo recipients within 42 days of any dose.

Seizures: All seizures reported in the phase 3 trials of RotaTeq (by vaccination group and interval after dose) for RotaTeq compared to placebo, respectively, were: days 1-7 (10 vs. 5), days 1-14 (15 vs. 8), and days 1-42 (33 vs. 24). Seizures reported as serious adverse experiences occurred in <0.1% (27/36,150) of vaccine and <0.1% (18/35,536) of placebo recipients (not significant). Ten febrile seizures were reported as serious adverse experiences, 5 were observed in vaccine recipients and 5 in placebo recipients.

Kawasaki Disease: In the phase 3 clinical trials, infants were followed for up to 42 days of vaccine dose. Kawasaki disease was reported in 5 of 36,150 vaccine recipients and in 1 of 35,536 placebo recipients with unadjusted relative risk 4.9 (95% CI 0.6, 239.1).

Most Common Adverse Events

Solicited Adverse Events: Detailed safety information was collected from 11,711 infants (6,138 recipients of RotaTeq) which included a subset of subjects in REST and all subjects from Studies 007 and 009 (Detailed Safety Cohort). A Vaccination Report Card was used by parents/guardians to record the child’s temperature and any episodes of diarrhea and vomiting on a daily basis during the first week following each vaccination. Table 3 summarizes the frequencies of these adverse events and irritability.

Table 3 Solicited adverse experiences within the first week after doses 1, 2, and 3 (Detailed Safety Cohort)						
Adverse experience	Dose 1		Dose 2		Dose 3	
	RotaTeq	Placebo	RotaTeq	Placebo	RotaTeq	Placebo
Elevated temperature [†]	n=5,616 17.1%	n=5,077 16.2%	n=5,215 20.0%	n=4,725 19.4%	n=4,865 18.2%	n=4,382 17.6%
	n=6,130 6.7%	n=5,560 5.4%	n=5,703 5.0%	n=5,173 4.4%	n=5,496 3.6%	n=4,989 3.2%
Vomiting						
Diarrhea	10.4%	9.1%	8.6%	6.4%	6.1%	5.4%
Irritability	7.1%	7.1%	6.0%	6.5%	4.3%	4.5%

[†]Temperature ≥100.5°F [38.1°C] rectal equivalent obtained by adding 1 degree F to otic and oral temperatures and 2 degrees F to axillary temperatures

Other Adverse Events: Parents/guardians of the 11,711 infants were also asked to report the presence of other events on the Vaccination Report Card for 42 days after each dose. Fever was observed at similar rates in vaccine (N=6,138) and placebo (N=5,573) recipients (42.6% vs. 42.8%). Adverse events that occurred at a statistically higher incidence (ie, 2-sided p-value <0.05) within the 42 days of any dose among recipients of RotaTeq (N=6,138) as compared with placebo (N=5,573) recipients, respectively, include: diarrhea (24.1% [n=1,479] vs. 21.3% [n=1,186], vomiting (15.2% [n=929] vs. 13.6% [n=758]), otitis media (14.5% [n=887] vs. 13.0% [n=724]), nasopharyngitis (6.9% [n=422] vs. 5.8% [n=325]), and bronchospasm (1.1% [n=66] vs. 0.7% [n=40]).

Safety in Pre-Term Infants: RotaTeq or placebo was administered to 2,070 pre-term infants (25 to 36 weeks gestational age, median 34 weeks) according to their age in weeks since birth in REST. All pre-term infants were followed for serious adverse experiences; a subset of 308 infants was monitored for all adverse experiences. There were 4 deaths throughout the study, 2 among vaccine recipients (1 SIDS and 1 motor vehicle accident) and 2 among placebo recipients (1 SIDS and 1 unknown cause). No cases of intussusception were reported. Serious adverse experiences occurred in 5.5% of vaccine and 5.8% of placebo recipients. The most common serious adverse experience was bronchiolitis, which occurred in 1.4% of vaccine and 2.0% of placebo recipients. Parents/guardians were asked to record the child’s temperature and any episodes of vomiting and diarrhea daily for the first week following vaccination. The frequencies of these adverse experiences and irritability within the week after dose 1 are summarized in Table 4.

Table 4 Solicited adverse experiences within the first week of doses 1, 2, and 3 among pre-term infants						
Adverse event	Dose 1		Dose 2		Dose 3	
	RotaTeq	Placebo	RotaTeq	Placebo	RotaTeq	Placebo
Elevated temperature [†]	N=127 18.1%	N=133 17.3%	N=124 25.0%	N=121 28.1%	N=115 14.8%	N=108 20.4%
	N=154 5.8%	N=154 7.8%	N=137 2.9%	N=137 2.2%	N=135 4.4%	N=129 4.7%
Vomiting						
Diarrhea	6.5%	5.8%	7.3%	7.3%	3.7%	3.9%
Irritability	3.9%	5.2%	2.9%	4.4%	8.1%	5.4%

[†]Temperature ≥100.5°F [38.1°C] rectal equivalent obtained by adding 1 degree F to otic and oral temperatures and 2 degrees F to axillary temperatures

Post-Marketing Experience: The following adverse events have been identified during post-approval use of RotaTeq from reports to the Vaccine Adverse Event Reporting System (VAERS). Reporting of adverse events following immunization to VAERS is voluntary, and the number of doses of vaccine administered is not known; therefore, it is not always possible to reliably estimate the adverse event frequency or establish a causal relationship to vaccine exposure using VAERS data. In post-marketing experience, the following adverse events have been reported in infants who have received RotaTeq: *Gastrointestinal disorders*—Intussusception (including death), Hematochezia. *Skin and subcutaneous tissue disorders*—Urticaria. *Infections and infestations*—Kawasaki disease.

Reporting Adverse Events: Parents or guardians should be instructed to report any adverse events to their health care provider. Health care providers should report all adverse events to the US Department of Health and Human Services’ Vaccine Adverse Events Reporting System (VAERS). VAERS accepts all reports of suspected adverse events after the administration of any vaccine, including but not limited to the reporting of events required by the National Childhood Vaccine Injury Act of 1986. For information or a copy of the vaccine reporting form, call the VAERS toll-free number at 1-800-822-7967 or report on line to www.vaers.hhs.gov.

DRUG INTERACTIONS

Immunosuppressive therapies including irradiation, antimetabolites, alkylating agents, cytotoxic drugs and corticosteroids (used in greater than physiologic doses), may reduce the immune response to vaccines.

Concomitant Vaccine Administration: In clinical trials, RotaTeq was administered concomitantly with diphtheria and tetanus toxoids and acellular pertussis (DTaP), inactivated poliovirus vaccine (IPV), H. influenzae type b conjugate (Hib), hepatitis B vaccine, and pneumococcal conjugate vaccine [see CLINICAL STUDIES]. The safety data available are in the ADVERSE REACTIONS section [see Clinical Studies Experience].

There was no evidence for reduced antibody responses to the diphtheria or tetanus toxoid components of DTaP or to the other vaccines that were concomitantly administered with RotaTeq. However, insufficient immunogenicity data are available to confirm lack of interference of immune responses when RotaTeq is concomitantly administered with childhood vaccines to prevent pertussis.

Pediatric Use: Safety and efficacy have not been established in infants less than 6 weeks of age or greater than 32 weeks of age. Data are available from clinical studies to support the use of RotaTeq in pre-term infants according to their age in weeks since birth. (See ADVERSE REACTIONS, Clinical Studies Experience.) Data are available from clinical studies to support the use of RotaTeq in infants with controlled gastroesophageal reflux disease.

Carcinogenesis, Mutagenesis, Impairment of Fertility: RotaTeq has not been evaluated for its carcinogenic or mutagenic potential or its potential to impair fertility.

Information for Parents/Guardians: Parents or guardians should be given a copy of the required vaccine information and be given the “Patient Information” appended to the Prescribing Information. Parents and/or guardians should be encouraged to read the patient information that describes the benefits and risks associated with the vaccine and ask any questions they may have during the visit. See PRECAUTIONS and Patient Information.

For more detailed information, please read the Prescribing Information.

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Manuf. and Dist. by:
MERCK & CO., INC. Whitehouse Station, NJ 08889, USA

Issued April 2008

Printed in USA

9714306