

A Survey of Pediatricians on the Reintroduction of a Rotavirus Vaccine

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ABSTRACT. *Objective.* Rhesus-based rotavirus tetravalent vaccine (RRV-TV; RotaShield) was withdrawn voluntarily from the market in October 1999, and recommendations for use were suspended. Rotavirus infection continues to be a significant health problem affecting children worldwide. The objective of this study was to investigate whether pediatricians would either reconsider using RRV-TV or consider other, newer, and presumably safer rotavirus vaccines if they were recommended routinely and to determine factors that influence their opinion.

Methods. A questionnaire was sent to a random sample of 250 members of the Wisconsin Chapter of the American Academy of Pediatrics (AAP) and to 437 randomly selected members of the Georgia Chapter of the AAP. Nonresponders received reminder questionnaires.

Results. Of the 687 pediatricians surveyed, 384 (56%) responded. Responses from 319 eligible immunization providers were included in the final analysis. Although only 15% of respondents reported that they would give RRV-TV if it were available today, 94% reported that they would use a new rotavirus vaccine if proved to be safer than RRV-TV and if recommended by the AAP and Advisory Committee on Immunization Practices for routine use among infants. Barriers to reintroducing a rotavirus vaccine were fear of adverse reactions among 95% of pediatricians, followed by potential high vaccine cost (63%) and amount of time required to educate parents (57%).

Conclusions. Pediatricians reported that they would use a rotavirus vaccine if it was safer than RRV-TV and routinely recommended by the AAP and the Advisory Committee on Immunization Practices. *Pediatrics* 2003;112:e6–e10. URL: <http://www.pediatrics.org/cgi/content/full/112/1/e6>; *rotavirus, rotavirus vaccine, RRV-TV.*

ABBREVIATIONS. RRV-TV, rhesus-based rotavirus tetravalent vaccine; AAP, American Academy of Pediatrics; ACIP, Advisory Committee on Immunization Practices.

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Rotavirus is the most common cause of severe diarrhea in young children worldwide. In the United States, 1 in 10 children with rotavirus disease will require an office or emergency department visit; 1 in 100 children will require hospitalization, and 1 in 200 000 will die as a result of rotavirus disease.¹ Outbreaks of disease as a result of rotavirus in child care centers are common.² In developing countries, the consequences are more severe, where an estimated 1 in 200 children die of complications from gastroenteritis as a result of rotavirus.³ Environmental factors, including clean water supplies and appropriate hygiene, do little to reduce the incidence of rotavirus diarrhea in either developed or developing countries.⁴

Rhesus-based rotavirus tetravalent vaccine ([RRV-TV] RotaShield; Wyeth Laboratories, Marietta, PA) was licensed and recommended for routine use among infants in the United States in 1998.^{1,5} After studies confirmed an increased risk of intussusception after first-dose vaccine administration to infants 2 to 3 months of age, RRV-TV was withdrawn voluntarily from the market in October 1999 and recommendations for use were suspended.^{6–8} Worldwide, the effect of the withdrawal of the immunization recommendation and the market withdrawal of RRV-TV has raised concerns about the future use of any rotavirus vaccine. This is a significant concern, especially in the developing world, where morbidity and mortality from rotavirus disease far exceed morbidity and mortality that occurs in developed countries.⁴

Anticipated use of a rotavirus vaccine by pediatricians is essential in development of future rotavirus vaccine policy. Educational efforts that address identifiable barriers to achieving practitioner advocacy will be necessary to ensure implementation of that policy. In collaboration with the Georgia and Wisconsin Chapters of the American Academy of Pediatrics (AAP), we conducted a survey of immunization providers on knowledge, attitudes, and past and anticipated practices surrounding rotavirus vaccine. The objectives of the study were 1) to determine whether pediatricians would reconsider using RRV-TV or consider other, newer, and presumably safer rotavirus vaccines if they were recommended and 2) to determine factors that influence their opinion.

METHODS

Subjects and Design

This study was a collaborative effort of the Georgia and Wisconsin Chapters of the AAP and the National Immunization Program. The Georgia Chapter of the AAP membership comprises approximately 80% of the practicing pediatricians in the state of Georgia (K. Townsend, personal communication, June 2001). Similarly, >90% of pediatricians in Wisconsin are in the Wisconsin Chapter of the AAP. By using 2 states in different areas of the country with different practice locations, we were better able to assess the opinions of divergent groups of pediatricians.

Georgia

Subjects were selected from the membership database of the Georgia Chapter of the AAP. The survey was conducted by 3 communication modes: postal mail, fax, and e-mail. Surveying physicians by these different modes was a separate research effort and is reported elsewhere.⁹ For targeting immunization providers, members listed as a subspecialist, retiree, government public health employee, or resident physician were excluded before sample selection. From the 1391 total members, 987 members were eligible. A total of 450 members were selected by a random-number generator program to receive the survey, 150 by postal mail, 150 by fax, and 150 by e-mail. Postal mail recipients were selected first, leaving 837 members. A total of 150 were chosen for fax recipients from the 488 who remained and had fax numbers listed. A total of 150 were chosen for the e-mail group from the remaining members who had e-mail addresses and had not been chosen for the fax or postal groups.

This study was reviewed and approved by the Human Investigations Committee of Emory University School of Medicine and the Institutional Review Board of the Centers for Disease Control and Prevention. A questionnaire and cover letter were sent to all sampled subjects in Georgia in July 2001. A follow-up reminder questionnaire was sent to nonresponders at 2 weeks after the initial mailing. The second reminder was sent 1 month after the initial mailing.

Wisconsin

In collaboration with the National Immunization Program, a similar questionnaire was sent by postal mail to pediatricians in Wisconsin. The questionnaire along with an explanatory cover letter was sent in December 2001 to 250 randomly selected members of the Wisconsin Chapter of the AAP. These physicians were selected from a pool of 550 Wisconsin pediatricians who had been identified as active in office-based practices through previous immunization-related physician surveys conducted in that state. Three weeks after posting of the initial survey, a follow-up postcard reminder was sent to 75 nonresponders without e-mail addresses, and e-mail reminders were sent to 43 nonresponders who had e-mail capabilities.

Survey Instrument

The questionnaire contained multiple-choice and Likert scale (rating scale from 1 to 5, 1 = strongly agree and 5 = strongly disagree) questions about practice setting, practice location, year of medical school graduation, patterns of referrals for children with severe gastroenteritis, attitudes about rotavirus disease in the United States and developing world, past and anticipated uses of a rotavirus vaccine, and perceived advantages and barriers to reintroducing a rotavirus vaccine. We inquired about anticipated use of RRV-TV and other, new rotavirus vaccines based on either permissive or routine recommendations from the AAP and the Advisory Committee on Immunization Practices (ACIP). Permissive vaccine use was defined in the survey as a vaccine available for use by individual clinicians who may select which children to vaccinate.

The questionnaire to Georgia pediatricians included questions on Internet usage and sources of vaccine information. Results of this part of the survey are reported elsewhere.⁹ A limited number of additional questions were included in the Wisconsin survey exploring pediatrician attitudes about postvaccination telephone calls from parents, availability of health resources to diagnose and treat infants with possible intussusception, and their knowledge of intussusception after first-dose RRV-TV. Except for a difference in

phrasing of 2 questions, the rotavirus and rotavirus vaccine-related questions in the 2 surveys were similar.

Only the Wisconsin pediatricians were made aware of the results of a September 2001 meeting convened by the National Vaccine Program Office and the National Vaccine Advisory Committee to assess and determine the incidence of intussusception after RRV-TV use. The distribution of the survey to Georgia pediatricians occurred before this meeting; therefore, Georgia survey participants were not aware of the estimated rate of intussusception. Any definition of "safer" as applied by Georgia respondents would have to be placed in the context of what a Georgia pediatrician may have heard from unpublished sources. Before the national rotavirus vaccine work group meeting, best estimates of intussusception after the use of RRV-TV initially were thought to be no more than 1 in approximately 5000 doses of vaccine administered. The age of vaccine recipients who developed intussusception and the rate and timing of intussusception after each of the 3 doses also were not known at the time of the Georgia survey.

Analysis

Respondents who did not provide immunizations, resident physicians, retired physicians, subspecialists, and public health workers were excluded in the final analysis to target immunization providers. Likert scale responses were collapsed into dichotomous variables to "strongly agree and agree" or "neutral, disagree, and strongly disagree." The questions in the 2 questionnaires were similar and allowed coalescing data for analysis and presenting combined results.

RESULTS

Response Rate and Eligibility

Georgia

Of the 450 selected pediatricians, 11 members had incorrect addresses and 2 were excluded before the survey was sent because they were identified as public health workers. A total of 437 pediatricians were sent surveys by post, fax, or e-mail. A total of 230 members responded for an overall response rate of 53%. Of these, 181 respondents were eligible and included in the final analysis of Georgia pediatricians. Forty-nine respondents were excluded from analysis because they indicated that they did not provide immunizations or were resident physicians, subspecialists, retired, or public health workers.

Wisconsin

A total of 250 questionnaires were sent to pediatricians throughout Wisconsin. Of these, 154 were returned, for a response rate of 62%. A total of 138 were identified as active immunization providers and were included in the final analysis. Sixteen respondents who did not provide immunization services were excluded.

The overall response rate of pediatricians from Georgia and Wisconsin was 56%. The final sample size collectively was 319, 46% of the total surveys sent. Characteristics of the eligible survey participants are listed in Table 1. There was a significant difference between Georgia and Wisconsin pediatricians in practice locations and number of pediatricians who graduated from medical school between 1950 and 1969. Annual pediatrician hospital and emergency department referrals for vomiting and diarrhea are shown in Fig 1.

Pediatrician Attitudes and Beliefs

Seventy-nine percent of surveyed pediatricians agreed or strongly agreed that rotavirus is a signifi-

TABLE 1. Respondent Characteristics of Pediatricians in Georgia and Wisconsin

Characteristic	Georgia % (n = 181)	Wisconsin % (n = 138)	P Value
Year of medical school graduation			
1950–1969	15	6	<.05
1970–1979	20	19	0.92
1980–1984	15	13	0.74
1985–1989	12	19	0.11
1990–1994	24	23	0.83
1995–1998	14	20	0.28
Practice location			
Rural	14	26	<.05
Suburban	57	45	<.05
Urban, inner-city	13	3	<.05
Urban, not inner-city	16	26	<.05

cant disease in the United States, and 95% of respondents believed that rotavirus diarrhea is a significant disease in the developing world. Ninety-four percent of pediatricians reported that new rotavirus vaccines should be proved safer than RRV-TV, with 49% identifying the safety characteristics of inactivated poliovirus vaccine as the most desirable profile for future rotavirus vaccines.

Pediatricians identified factors that would affect their decision to reintroduce a rotavirus vaccine. Eighty-three percent of pediatricians agreed or strongly agreed that decreased morbidity, expressed as a decrease in number of patients hospitalized with diarrhea and dehydration, would be an important factor that would influence their decision. Potential barriers to reintroduction included fear of adverse reactions among 95% of respondents, concerns of high vaccine cost reported among 63% of respondents, and the time required to educate parents reported by 57% of respondents (Fig 2). A factor that was not considered to be important by both Georgia and Wisconsin pediatricians was adverse pressure from antivaccine groups.

Fifty percent of Wisconsin pediatricians indicated that telephone calls from parents concerning irritability, vomiting, or colicky behavior in recently immunized infants and the lack of community resources for diagnosis and treatment of potential

vaccine-related intussusception made reintroducing a rotavirus vaccine problematic. Sixty-three percent of Wisconsin pediatricians who practice in rural settings were concerned about access to radiologic and surgical services in the event of a postvaccination intussusception episode in a 2- to 3-month-old infant.

Past and Anticipated Practices of Rotavirus Vaccines

Sixty-eight percent of respondents indicated that they had used RRV-TV in the past, with 53% giving the vaccine routinely to all eligible infants in their practice. Only 15% of Georgia and Wisconsin pediatricians reported that they would give RRV-TV if it were available today (Table 2). Although pediatricians might not want to use RRV-TV in the United States, 75% of Georgia pediatricians believed that RRV-TV should be used in developing countries. (This question was not included in the survey of Wisconsin pediatricians.)

Fifty-one percent of Georgia pediatricians reported that they would give RRV-TV if it were found safer and if the AAP and the ACIP recommended permissive use. Seventy-two percent would use RRV-TV if it were found safer and if routine use were recommended by the AAP and the ACIP. Knowing the estimated 1 in 10 000 intussusception rate after first-dose RRV-TV use in 2- to 3-month-old infants, 32% of Wisconsin pediatricians reported that they would give RRV-TV if recommended for permissive or routine use.

If there were a new rotavirus vaccine that was found to be safer than RRV-TV and recommended for permissive use by the AAP and the ACIP, 80% of surveyed pediatricians responded that they would use it. If a new, safer rotavirus vaccine were routinely recommended by the AAP and the ACIP, 93% of surveyed pediatricians would use it.

DISCUSSION

Findings from our investigation suggest that the overwhelming majority of pediatricians who participated in this study consider rotavirus to be a significant disease in the United States and worldwide. Similarly, they are interested in using a new, rotavirus vaccine if it were proved to be safer than RRV-TV and if the vaccine were recommended for routine use among children by the AAP and the ACIP. The rotavirus vaccine cost/benefit profile and the time required to discuss rotavirus vaccine use and the risk of potential low-frequency serious adverse events with parents were considered important issues that would have to be addressed for pediatricians to be strong advocates for routine use.

This study provides important information about development of vaccine policies and education about these policies. Recommendations from the AAP and the ACIP, the main sources of vaccine information that both the Georgia and Wisconsin pediatricians identified, did influence opinions for vaccine use. Most pediatricians surveyed in both states preferred routine to permissive recommendations and were more likely to use a vaccine given routine recommendations. For the AAP and the ACIP to confidently recommend future use of a rotavirus vaccine,

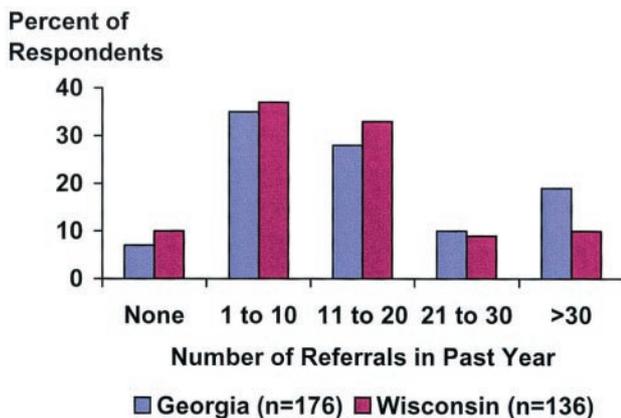


Fig 1. Referrals by Georgia and Wisconsin pediatricians to a hospital or emergency department for children with vomiting and diarrhea in the past year.

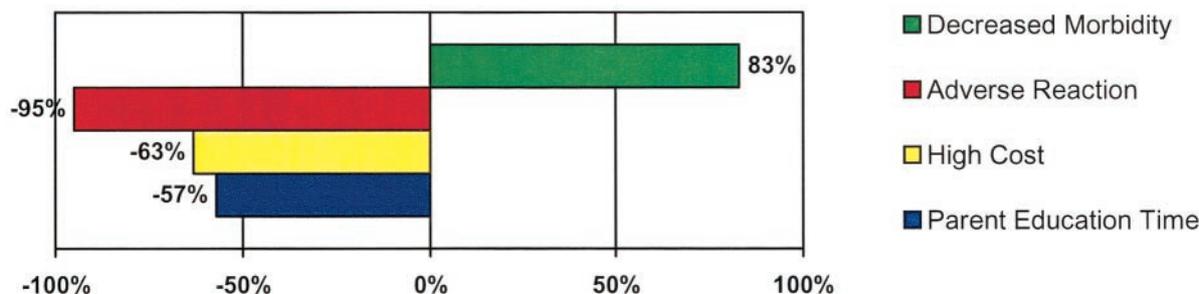


Fig 2. The impact of various factors on the decision of pediatricians from Georgia and Wisconsin to the introduction of a new rotavirus vaccine

physician and public fear of postvaccination adverse reactions, the time required to educate parents about a new vaccine, and the impact of vaccine cost would have to be addressed.

The need to reduce morbidity and mortality from rotavirus diseases warrants availability of a rotavirus vaccine in the absence of any specific treatment modality for rotavirus infection. However, concerns about the frequency and severity of adverse reactions to vaccines strongly influence the way pediatricians practice and how strong an advocate they can be for the use of a vaccine. The biggest potential barrier among surveyed pediatricians to the reintroduction of a rotavirus vaccine seems to be the fear of an adverse reaction such as intussusception. A benchmark for the incidence of an adverse event such as intussusception was addressed in the Wisconsin survey, in which an expressed rate of 1 episode of intussusception in 10 000 first doses of RRV-TV given to 2- to 3-month-old infants seemed to be viewed as a significantly negative influence on recommending RRV-TV for their patients. This impression seemed to be of sufficient importance that 68% of Wisconsin pediatricians would not follow an AAP or ACIP recommendation approving permissive or routine use of RRV-TV. However, the antici-

pated use of a new, presumably safer rotavirus vaccine received 93% approval of surveyed pediatricians. A previous survey of pediatricians and family practitioners on the effect of the withdrawal of RRV-TV on physicians' trust in vaccine safety mechanisms showed that one third of physicians would not use a rotavirus vaccine that was recommended for routine use until it had been in widespread use for months to years, indicating a potential delay in implementation of an approved and recommended future rotavirus vaccine.¹⁰

An ongoing discussion concerns the relative risk of intussusception after RRV-TV administration and the impact that this should have on other rotavirus vaccines currently in clinical trials. Any reintroduction of other rotavirus vaccines should favor a safer vaccine with a vaccine-associated intussusception rate well below the 1 in 10 000 occurrence attributable to RRV-TV. However, the question remains as to what is that acceptable level of risk of intussusception for practicing pediatricians.

The strengths of this study include the uniformity of opinions among physicians in the 2 states and the collaboration with state chapters of the AAP. Limitations include the large number of incorrect addresses encountered. The survey to the Georgia pe-

TABLE 2. Select Questions and Responses of Wisconsin and Georgia Pediatricians on Their Anticipated Use of a Rotavirus Vaccine

	Wisconsin (%)	Georgia (%)	Total (%)
If RotaShield in its original form were available today, would you give this vaccine?	16.5	13.4	14.7
If original RotaShield were found safer and if permissive use is recommended by AAP and ACIP, would you give RotaShield?		51.4	
If original RotaShield were found safer and if routine use is recommended by AAP and ACIP, would you give RotaShield?		71.7	
Knowing the current safety profile of the original RotaShield and if permissive use were to be recommended by AAP and ACIP, would you give RotaShield?	31.6		
Knowing the current safety profile of the original RotaShield and if routine use were to be recommended by AAP and ACIP, would you give RotaShield?	32.3		
If there were a new, safer rotavirus vaccine and permissive use is recommended by AAP and ACIP, would you give this vaccine?	80.1	79.5	79.8
If there were a new, safer rotavirus vaccine and routine use is recommended by AAP and ACIP, would you give this vaccine?	89.6	95.5	92.9

pediatricians involved 3 communication modes—postal mail, e-mail, and fax. It is unknown how this may have affected response rate and response bias. Because respondents were informed that the questionnaire was from the state chapters of the AAP and the Centers for Disease Control and Prevention, this may have introduced bias by affecting the way that they responded to questions. Although we have limited information on nonresponders to compare with responders, the unexpectedly high proportion of pediatricians in Georgia and Wisconsin who reported offering RRV-TV routinely to eligible infants in their practices may be biased by survey responders who felt compelled to participate in the survey. Similarly, pediatricians who are not interested in the vaccine or did not use the vaccine may have had less reason to participate actively in the survey. In addition, baseline knowledge differences for the 2 physician groups polled will have a strong influence on the response to certain questions regarding safety, but any differences can be expected to provide more insight into the specifics of physician acceptance of adverse event levels.

CONCLUSIONS

Pediatricians reported that they would use a rotavirus vaccine if it was safer than RRV-TV and was recommended for routine use by the AAP and the ACIP. An intussusception rate of 1:10 000 first doses given to 2- to 3-month-old infants seems to be excessive based on responses from Wisconsin pediatricians who were provided with this information. For a rotavirus vaccine to be reintroduced successfully, potential barriers to overcome include fear of adverse events, high vaccine cost, time needed to educate parents, and availability of facilities to diagnose rare adverse events such as intussusception. We conclude from this study that research efforts must be

geared toward development of rotavirus vaccines that have efficacy and safety profiles that reassure trusted national recommending organizations, such as the AAP, the American Academy of Family Practitioners, and the ACIP, to recommend confidently their routine use among infants and young children.

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REFERENCES

- Centers for Disease Control and Prevention. Rotavirus vaccine for the prevention of rotavirus gastroenteritis among children: recommendations of the Advisory Committee on Immunization Practices. *MMWR Morb Mortal Wkly Rep.* 1999;48(RR-2):1–20
- Pickering LK, Cordell RL. Infectious diseases associated with out-of-home childcare. In: Long SS, Pickering LK, Prober CG, eds. *Principles and Practice of Pediatric Infectious Diseases.* Philadelphia, PA: Churchill-Livingstone; 2002:27–33
- Cicirello HG, Glass RI. Current concepts of the epidemiology of diarrheal disease. *Semin Pediatr Infect Dis.* 1994;5:163–167
- Parashar UD, Bresee JS, Gentsch J, Glass RI. Rotavirus. *Emerg Infect Dis.* 1998;4:561–568
- American Academy of Pediatrics, Committee on Infectious Diseases. Prevention of rotavirus disease: guidelines for use of rotavirus vaccine. *Pediatrics.* 1998;102:1483–1491
- Centers for Disease Control and Prevention. Intussusception among recipients of rotavirus vaccine—United States, 1998–1999. *MMWR Morb Mortal Wkly Rep.* 1999;48:577–581
- Centers for Disease Control and Prevention. Withdrawal of rotavirus vaccine recommendation. *MMWR Morb Mortal Wkly Rep.* 1999;48:1007
- Murphy TV, Gargiullo PM, Massoudi MS, et al. Intussusception among infants given an oral rotavirus vaccine. *N Engl J Med.* 2001;344:564–572
- McMahon SR, Iwamoto M, Massoudi MS, et al. Comparison of e-mail, fax, and postal surveys of pediatricians. *Pediatrics.* 2003;111(4). Available at: www.pediatrics.org/cgi/content/full/111/4/e299
- McPhillips HA, Davis RL, Marcuse EK, Taylor JA. The rotavirus vaccine's withdrawal and physicians' trust in vaccine safety mechanisms. *Arch Pediatr Adolesc Med.* 2001;155:1051–1056

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