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## Rotavirus Update: RotaTeq Is Effective, and a Second Vaccine Has Been Approved



In collaboration with:  
**The Saudi Paediatric Association**, P.o.Box: 2925 - Riyadh  
11461  
Tel: (01)467-1507 / 205-0491  
Fax: (01)467-1570 / 205-0391

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See next page

*The 2007–2008 rotavirus activity was delayed in onset and diminished in magnitude, compared with previous seasons.*

RotaTeq, the first licensed rotavirus vaccine, was recommended by the CDC for routine use in infants in February 2006. To examine the incidence of rotavirus during the subsequent winter and spring, the CDC used data from the National Respiratory and Enteric Virus Surveillance System (NREVSS) and the New Vaccine Surveillance Network (NVSN).

Based on NREVSS weekly reports of rotavirus tests (enzyme immunoassays), onset of rotavirus activity was 2 to 4 months earlier during prevaccine seasons (July 1991 through June 2006) than during the 2008 season (mid-November to late February). The percentage of positive rotavirus tests during prevaccine periods peaked by March (range, 30.6% to 45.5%). In 2008, the percentage of positive tests peaked in April at only 17.8%.

Based on prospective NVSN data for rotavirus gastroenteritis in children younger than 3 years from three U.S. counties, the percentage of submitted stools that tested positive for rotavirus from January 1 to April 30 declined from 51% in 2006 and 54% in 2007 to 6% in 2008.

A second rotavirus vaccine, Rotarix, was approved in early 2008 and should be available later this year. Practitioners might want to know the differences between the two vaccines: RotaTeq is a bovine recombinant vaccine that is licensed as a three-dose oral regimen; Rotarix contains an attenuated human strain and is licensed as a two-dose oral regimen. Both vaccines have been shown to be safe and efficacious in large clinical trials — RotaTeq against rotavirus gastroenteritis serotypes G1–4 and Rotarix against rotavirus gastroenteritis G1. New provisional recommendations from the Advisory Committee on Immunization Practices (ACIP) advise use of either vaccine for routine vaccination and do not state a preference. However, the ACIP recommends using the same product for the complete vaccine series, when possible. If both products must be used, three doses of rotavirus vaccine are required.

**Comment:** Kudos to the pediatric community for having a major effect on this vaccine-preventable disease. The Vaccine Adverse Event Reporting System has not found any increase in intussusception with RotaTeq, as some had feared. The combined safety and efficacy data should be reassuring to families concerned about the risk-benefit ratio. Let's keep up the good work.

— Peggy Sue Weintrub, MD

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*FDA approves new vaccine to prevent gastroenteritis caused by rotavirus [press release]. Rockville, MD : Food and Drug Administration; Apr 3 , 2008. (<http://www.fda.gov/bbs/topics/NEWS/2008/NEW01814.html>)*

## Retesting Adopted Children for Tuberculosis

*Repeat TB testing is necessary for internationally adopted children.*

For internationally adopted children who come to the U.S., is retesting necessary for those whose initial tuberculin skin tests (TSTs) are negative? To find out, investigators evaluated 527 such children (mean age, 23 months); most were adopted from Russia, China, or Guatemala.

On initial testing within 2 months of arrival, 416 children (79%) had negative TSTs, and 111 children (21%) had positive TSTs (10 mm induration). None of the children with positive tests had evidence of active tuberculosis (TB) infection. Of 204 children with initial negative results who were retested at least 3 months after their initial tests, 191 were read within 48 to 72 hours, and 38 were positive; again, none had active TB infections. Presence of a bacille Calmette-Guérin (BCG) immunization scar and better nutritional status (assessed by weight for age) were related significantly to a positive TST result on initial testing. Improved nutritional status also was associated with a positive TST result on repeat testing.

**Comment:** Even if we assume negative results for all children who were not retested and for those whose tests were not read within 48 to 72 hours, the positive rate at retesting would be 9% (38 of 416). The authors speculate that improved nutrition after coming to the U.S., with reversal of anergy, might account for some of the positive retest results. Although some positive tests might represent reactions to BCG, these data indicate clearly that repeat testing for TB is necessary in internationally adopted children.

— Howard Bauchner, MD

### CITATION(S):

*Trehan I et al. Tuberculosis screening in internationally adopted children: The need for initial and repeat testing. Pediatrics 2008 Jul; 122:e7. (<http://dx.doi.org/10.1542/peds.2007-1338>)*

## Exercise plus Amenorrhea Equals Thinner Bones

*Adolescent endurance athletes with amenorrhea had significantly lower BMD z scores than did either eumenorrheic athletes or eumenorrheic nonathletes.*



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8. Institute of medicine. Dietary reference intakes for vitamin C, vitamin E, selenium and carotenoids, food and nutrition board. Washington DC: National Academy Press; 2005.

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Although one benefit of exercise is increased bone-mineral density (BMD), female adult athletes with amenorrhea have low BMD. To examine whether the same is true for female adolescent athletes (age range, 12–18 years), researchers in Boston compared BMD, body composition, and insulin-like growth factor 1 (IGF-1) levels in 21 adolescent athletes with amenorrhea, 18 athletes with normal menstruation, and 18 controls who were not athletes and did not have amenorrhea.

Athletes reported one of the following: at least 4 hours per week of aerobic weight training of the legs, more than 30 miles per week of running, or more than 4 hours per week of endurance training for at least 6 months. Athletes with amenorrhea had missed at least three consecutive cycles following at least 6 months of regular cycles or did not reach menarche by age 15.3 years.

Athletes with amenorrhea had significantly lower BMD z scores (measured by dual-energy radiograph absorptiometry) at the spine and whole body than either eumenorrheic athletes or controls and significantly lower hip BMD z scores than eumenorrheic athletes. Lean mass did not differ among the three groups, but athletes with amenorrhea had lower BMI z scores than eumenorrheic athletes and lower IGF-1 levels than controls. Markers of bone turnover were significantly lower in amenorrheic athletes than in controls. Activity scores were greater for athletes with and without amenorrhea than for controls.

**Comment:** This study underscores the risk associated with amenorrhea in adolescent athletes and the importance of maintaining regular menses. Unfortunately, the activity questionnaire did not measure energy expenditure so the authors could not determine whether low BMI, increased energy drain, or both lead to amenorrhea. Until this is clarified, athletes must be advised to increase their caloric intake until menses are restored, even if that means an increase in BMI. Although oral contraceptives will restore menses, whether contraceptives enhance bone density is uncertain; therefore, contraceptive use might falsely reassure athletes.

— Alain Joffe, MD, MPH, FAAP

**CITATION(S):**

*Christo K et al. Bone metabolism in adolescent athletes with amenorrhea, athletes with eumenorrhea, and control subjects. Pediatrics 2008 Jun; 121:1127.*

*In a large population-based study, children with simple febrile seizures did not have higher risk for death, but children with complex seizures did.*

Mortality risk associated with febrile seizures in children is uncertain. Investigators examined this risk in a population-based study of more than 1.6 million Danish children born in 1977 through 2004 and followed for as long as 28 years (23.1 million person-years).

Compared with children without histories of febrile seizures, the 55,215 children with a first febrile seizure between ages 3 months and 5 years had mortality rate ratios (MRRs) that were 80% higher during the first postictal year, 90% higher during the second year, and similar to the general population thereafter. Risk for sudden unexplained death during the 2 years after a first febrile seizure

## No Increase in Long-Term Mortality After Simple Febrile Seizures

(either simple or complex) was five times higher than in the general population, although the absolute risk was low (11 deaths per 100,000 children). Cause-specific MRRs during the 2 years after a first febrile seizure were highest for children who had seizures during the first year of life and those with central nervous system malformations or infections. In a nested case-control study, mortality among children with simple febrile seizures (15 minutes without recurrence within 24 hours) was similar to the rate in the general population (MRR, 1.09), but mortality was higher among children with complex seizures (>15 minutes with recurrence within 24 hours; MRR, <1.99), particularly those with preexisting neurologic abnormalities and subsequent epilepsy.

**Comment:** This large population study indicates that simple febrile seizures are not associated with significantly higher risk for death during the first 3 decades of life. An editorialist also notes that the findings refute an association between simple febrile seizures and sudden infant death. He emphasizes the importance of these results in reassuring parents of children with simple febrile seizures and suggests that children with complex febrile seizures and neurologic abnormalities require surveillance and extended follow-up.

— F. Bruder Stapleton, MD

**CITATION(S):**

Vestergaard M et al. Death in children with febrile seizures: A population-based cohort study. *Lancet* 2008 Aug 9; 372:457.

Mazumdar M. Febrile seizures and risk of death. *Lancet* 2008 Aug 9; 372:429.

*Immunodeficiency can present in patients of any age.*

Common variable immunodeficiency (CVID) refers to a constellation of acquired B-cell disorders that have similar presentations and laboratory findings. Patients with CVID have recurrent infections with encapsulated organisms as well as chronic gastrointestinal, skin, and soft-tissue infections. Some patients have combined B- and T-cell dysfunction that can lead to autoimmune problems and an increased risk for malignancy. The estimated prevalence of CVID is 1 case per 30,000 whites, but the disease might be underdiagnosed. In this study, researchers examined clinical characteristics of 252 adult patients with CVID (56% female; 90% white) who were enrolled from 2004 through 2007 in a French national study of adults with primary hypogammaglobulinemia. Clinical events before study entry were retrospectively analyzed.

The median age at symptom onset was 19 years; however, 40% of patients had symptoms before age 15, and 14% had symptoms before age 5. Median delay of diagnosis was 16 years for patients with onset of symptoms before 1990 and has decreased to 3 years for patients with onset after 1990. Upper respiratory tract infection (including sinusitis and bronchitis) was the most common initial symptom, and pneumonia was the symptom that most often prompted diagnostic evaluation for CVID. Only 6% of patients developed opportunistic infections. Other common symptoms included splenomegaly (38%), chronic diarrhea (23%), autoimmune cytopenia (18%), and other autoimmune disorders (16%).

## Presentation and Diagnosis of Common Variable Immunodeficiency

## Use of Soy-Based Formulas in Infants: Myths, Misuse, and Misconceptions

**Comment:** Many patients in this cohort experienced symptoms during childhood but did not receive a diagnosis until adulthood. More childhood cases would have been detected if the screening network had included children. Most practitioners think of immunodeficiencies as disorders that present most often in male infants. However, CVID should be considered in older children of either sex who have refractory infections or symptoms. Analysis of immunoglobulins (IgG, IgA, and IgM) and an HIV test can rule out or confirm the diagnosis, and early treatment can be initiated if abnormalities are detected.

— Peggy Sue Weintrub, MD

**CITATION(S):**

Oksenhendler E et al. *Infections in 252 patients with common variable immunodeficiency. Clin Infect Dis* 2008 May 15; 46:1547.

*An updated clinical report reviews the contraindications and limited indications for soy formula in infants.*

Soy protein-based formulas are approved by the FDA for infants and account for about 20% of the U.S. formula market. Soy formulas are free of cow's milk protein and lactose and differ from cow's milk-based formulas in several ways: The carbohydrate sources are sucrose and corn-based polysaccharides; the protein source is a soy isolate supplemented with amino acids; and the formulas are fortified with additional calcium, phosphorus, iron, and zinc to overcome the binding of these minerals by soy phytate.

The AAP Committee on Nutrition recently released a statement on the effects of early nutritional interventions on the development of atopic disease. Now, the Committee on Nutrition has updated its 1998 statement on the use of soy protein-based formulas in infant feeding.

Key points from this clinical report include the following:

- Indications for soy protein-based formulas are limited to inborn errors of lactose metabolism, such as galactosemia and primary lactase deficiency, and the desire to provide a diet free of animal products.
- For treatment of infants with acute diarrhea, some studies report faster recovery when soy formula is substituted for lactose-containing formula to manage secondary, transient lactase deficiency, but the evidence is inconclusive. Other options include use of cow's milk formulas with reduced or no lactose. Following rehydration, most infants can be continued on breast milk or cow's milk formula.
- Soy formulas are not recommended for preterm infants.

The report clarifies many misconceptions about use of soy protein-based formula, including the following:

- Colic: Soy formula has no proven benefit in infants with colic.
- Cow's milk protein-induced enterocolitis or allergy: Many infants with cow's milk protein-induced enterocolitis or allergy also have soy allergy. A hydrolyzed protein formula should be given to these children.



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#### IMPORTANT NOTICE:

The World Health Organisation (WHO) has recommended that pregnant women and new mothers be informed of the benefits and superiority of breastfeeding - in particular the fact that it provides the best nutrition and protection from illness for babies. The Global Strategy for Infant and Young Child Feeding adopted by the 2002 World Health Assembly states that "as a global public health recommendation, infants should be exclusively breastfed for the first six months of life to achieve optimal growth, development and health." Mothers should be given guidance on the preparation for, and maintenance of, lactation, with special emphasis on the importance of a well-balanced diet both during pregnancy and after delivery. Unnecessary introduction of partial bottle-feeding or other foods and drinks should be discouraged since it will have a negative effect on breastfeeding. Similarly, mothers should be warned of the difficulty of reversing a decision not to breastfeed. Before advising a mother to use an infant formula, she should be advised of the social and financial implications of her decision; for example, if a baby is exclusively bottle-fed, more than one can (400g) per week will be needed, so the family circumstances and costs should be kept in mind. Mothers should be reminded that breast milk is not only the best, but also the most economical food for babies. If a decision to use an infant formula is taken, it is important to give instructions on correct preparation methods, emphasising that un-boiled water, unsterilised bottles or incorrect dilution can all lead to illness.

\* See: International Code of Marketing of Breast Milk Substitutes, adopted by the World Health Assembly in Resolution WHA 34.22, May 1981.

Information for medical profession only

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- Prevention of atopic disease: Soy formula does not prevent atopic disease in high-risk infants.
- Peanut allergy: Evidence of a link between soy formula and peanut allergy is contradictory.
- Phytoestrogens: No conclusive evidence exists that phytoestrogens (particularly isoflavones), which are present in soy formula, cause reproductive, endocrine, or developmental dysfunction.

**Comment:** This statement clearly limits the role of soy-based formula in infant feeding to infants with galactosemia and hereditary lactase deficiency. Soy formula rarely is necessary after rehydration in infants with diarrhea, should not be used in infants with cow's milk protein allergy because of cross-reactivity, and has no role in the management of colic or prevention of allergic disease. Based on the information provided in this report, the popularity of soy formula seems unjustified, and concerns about the effects of soy formula phytoestrogens might be exaggerated. In addition, the use of sucrose as the carbohydrate source in soy formulas is controversial. Pediatricians should consider this information when counseling families and making recommendations for infant feeding.

— Howard Bauchner, MD, and Cornelius W. Van Niel, MD

**CITATION(S):**

Bhatia J et al. for the American Academy of Pediatrics Committee on Nutrition. Use of soy protein-based formulas in infant feeding. *Pediatrics* 2008 May; 121:1062.

*Risks for medical and social disabilities increased with decreasing gestational age.*

Increasing survival of very premature infants has led to concern about adult outcomes. In the largest and longest follow-up study to date, investigators in Norway used linked data from national registries to examine adult outcomes of nearly 1 million infants (gestational age, 23 weeks) who were born without congenital anomalies between 1967 and 1983 and followed through 2003 (age, 20 to 36 years).

The prevalence of virtually all adverse medical and social outcomes, except for measures of criminality, increased with decreasing gestational age. For example, the prevalence of mental retardation was 4.4% among 1822 adults born at 23 to 27 weeks' gestation compared with 0.5% among those born at term, and the prevalence of cerebral palsy was 9.1% compared with 0.1%, respectively. The prevalence of autistic spectrum disorder (ASD) was 0.6% among those born at 23 to 27 weeks, 0.4% among 2805 adults born at 28 to 31 weeks, and 0.05% among those born at term. Only 25% of adults born at 23 to 27 weeks received university degrees versus 35% of adults born at term. The prevalence of low job-related income also increased with decreasing gestational age. Gestational age was not associated with sentencing for violent crimes or drug felonies.

**Comment:** These data reinforce that primary care providers should be vigilant about detection of ASD and mental retardation among children who are born very prematurely. The study also suggests that, although very premature infants have poorer medical and economic outcomes than their peers, most function

## How Do Premature Infants Function as Adults?

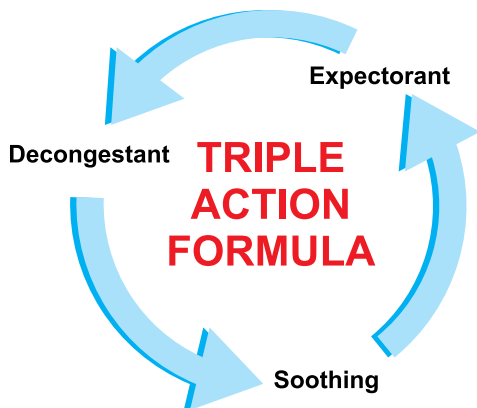
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## If You Give Sick Kids Their Shots, Will They Return for Well-Child Visits?

well as adults. Reassuringly, no differences emerged in any measure of criminality.

— Howard Bauchner, MD

### CITATION(S):

Moster D et al. Long-term medical and social consequences of preterm birth. *N Engl J Med* 2008 Jul 17; 359:262.

*Immunizing children at sick visits reduces the likelihood that they will return for well-child care.*

Vaccination rates can be improved if children receive vaccines at opportunities outside of routine well-child care, such as at sick visits. Investigators retrospectively examined the effect of immunization at sick visits on subsequent attendance at well-child visits among all 1675 children (85% black, 75% without private insurance) who were born in 2003–2004 and were seen at four urban clinics in Philadelphia.

In analyses of a wide range of demographic and health-related factors, vaccination at a sick visit (total outpatient sick visits, 4845) had the greatest effect on return for upcoming well-child care: Children who received vaccines were 45% less likely to return for a well-child visit within 60 days than children who were not vaccinated. In multivariate analyses, among children who were due (but not overdue) for vaccines at the time of the sick visit, 73% of children who did not receive the vaccine returned for well-child care versus 42% of those who were vaccinated. Among children who were overdue for vaccines at the sick visit, 47% of children who were not vaccinated returned for well-child care versus 31% of those who were vaccinated. Of the five well-child visits recommended between ages 6 weeks and 13 months, children who never received shots at sick visits averaged 3.8 well-child visits, those vaccinated at one sick visit averaged 3.3 well-child visits, and those vaccinated at more than one sick visit averaged 2.8 well-child visits.

**Comment:** Although capitalizing on vaccination opportunities is important, these results suggest that an unintended consequence of immunizing children at sick visits might be incomplete well-child care, at least in low-income urban populations. One consequence of coordinating vaccine schedules with well-child care is that many caregivers consider vaccination as the primary reason for well-child visits. Vaccines can be given at sick visits, but pediatricians must emphasize the importance of returning for routine well-child visits by previewing emerging issues to be discussed at upcoming visits such as safety, nutrition, development, and behavior.

— Cornelius W. Van Niel, MD

### CITATION(S):

Fiks AG et al. Impact of immunization at sick visits on well-child care. *Pediatrics* 2008 May; 121:898.

## Playground Injuries: Children Need to Play . . . Safely

*Monkey bars cause the most playground injuries.*

Given the risk for obesity in U.S. children, they need to stay active, but they also need to be protected from injury. The author of this study used the National Electronic Injury Surveillance System (NEISS) database of emergency department (ED) visits in 2002 through 2004 to investigate injuries associated with playground equipment in children younger than 18 years.

Of 22,278 ED visits for playground injuries by 17,700 children (54% boys; mean age, 6.5 years), 45% of visits involved monkey bars, 30% involved swings, and 25% involved slides. The most frequent injuries were fractures (44%), followed by contusions-abrasions (22%), lacerations (15%), strains and sprains (10%), and traumatic brain injuries (TBIs; 9%). Monkey bars were the most common cause of fractures, and swings were the most common cause of TBIs. Nearly 40% of injuries occurred at school, 35% occurred at recreation-sporting facilities, and 25% occurred at home. Most children (94%) who were seen in the ED were treated and released. The overall incidence of playground equipment injuries peaked in the summer, and the incidence of such injuries at school peaked in the spring and fall. Based on NEISS data since 1991, the frequency of injuries associated with swings and slides has decreased, but the frequency of injuries caused by monkey bars has not. Children with fractures were nearly 10 times more likely and children with TBIs were 5 times more likely to be admitted than children with contusions.

**Comment:** I don't think we can make active play risk free, but we can certainly use data such as these to identify ways to reduce risk. Supervised play at school along with height limitations and soft landing surfaces for monkey bars might reduce both the number and the severity of injuries, but we certainly should not use these data to reduce children's opportunities to play.

— William P. Kanto, Jr., MD

**CITATION(S):**

Loder RT. The demographics of playground equipment injuries in children. *J Pediatr Surg* 2008 Apr; 43:691.

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AA: Arachidonic acid. DHA: Docosahexaenoic acid.

Breast milk is best for babies. Infant formula is intended to replace breast milk when mothers do not breast-feed. Good maternal nutrition is important for preparation and maintenance of breast-feeding. Introducing partial bottle-feeding could negatively affect breast-feeding and reversing a decision not to breast-feed is difficult. Professional advice should be followed on infant feeding. Infant formula should be prepared and used as directed. Unnecessary or improper use of infant formula may present a health hazard. Social and financial implications should be considered when selecting a method of infant feeding.

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