PEDIATRICS[®]

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Febrile Seizures: Guideline for the Neurodiagnostic Evaluation of the Child With a Simple Febrile Seizure

Subcommittee on Febrile Seizures *Pediatrics* 2011;127;389 DOI: 10.1542/peds.2010-3318

The online version of this article, along with updated information and services, is located on the World Wide Web at:

http://pediatrics.aappublications.org/content/127/2/389.full.html

PEDIATRICS is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. PEDIATRICS is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2011 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0031-4005. Online ISSN: 1098-4275.



Organizational Principles to Guide and Define the Child Health Care System and/or Improve the Health of all Children

Clinical Practice Guideline—Febrile Seizures: Guideline for the Neurodiagnostic Evaluation of the Child With a Simple Febrile Seizure

SUBCOMMITTEE ON FEBRILE SEIZURES

KEY WORD

seizure

ABBREVIATIONS

AAP—American Academy of Pediatrics Hib—*Haemophilus influenzae* type b

EEG-electroencephalogram

CT—computed tomography

The recommendations in this report do not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate.

This document is copyrighted and is property of the American Academy of Pediatrics and its Board of Directors. All authors have filed conflict of interest statements with the American Academy of Pediatrics. Any conflicts have been resolved through a process approved by the Board of Directors. The American Academy of Pediatrics has neither solicited nor accepted any commercial involvement in the development of the content of this publication.

www.pediatrics.org/cgi/doi/10.1542/peds.2010-3318 doi:10.1542/peds.2010-3318

All clinical practice guidelines from the American Academy of Pediatrics automatically expire 5 years after publication unless reaffirmed, revised, or retired at or before that time.

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

Copyright © 2011 by the American Academy of Pediatrics

abstract



OBJECTIVE: To formulate evidence-based recommendations for health care professionals about the diagnosis and evaluation of a simple febrile seizure in infants and young children 6 through 60 months of age and to revise the practice guideline published by the American Academy of Pediatrics (AAP) in 1996.

METHODS: This review included search and analysis of the medical literature published since the last version of the guideline. Physicians with expertise and experience in the fields of neurology and epilepsy, pediatrics, epidemiology, and research methodologies constituted a subcommittee of the AAP Steering Committee on Quality Improvement and Management. The steering committee and other groups within the AAP and organizations outside the AAP reviewed the guideline. The subcommittee member who reviewed the literature for the 1996 AAP practice guidelines searched for articles published since the last guideline through 2009, supplemented by articles submitted by other committee members. Results from the literature search were provided to the subcommittee members for review. Interventions of direct interest included lumbar puncture, electroencephalography, blood studies, and neuroimaging. Multiple issues were raised and discussed iteratively until consensus was reached about recommendations. The strength of evidence supporting each recommendation and the strength of the recommendation were assessed by the committee member most experienced in informatics and epidemiology and graded according to AAP policy.

conclusions: Clinicians evaluating infants or young children after a simple febrile seizure should direct their attention toward identifying the cause of the child's fever. Meningitis should be considered in the differential diagnosis for any febrile child, and lumbar puncture should be performed if there are clinical signs or symptoms of concern. For any infant between 6 and 12 months of age who presents with a seizure and fever, a lumbar puncture is an option when the child is considered deficient in *Haemophilus influenzae* type b (Hib) or *Streptococcus pneumoniae* immunizations (ie, has not received scheduled immunizations as recommended), or when immunization status cannot be determined, because of an increased risk of bacterial meningitis. A lumbar puncture is an option for children who are pretreated with antibiotics. In general, a simple febrile seizure does not usually require further evaluation, specifically electroencephalography, blood studies, or neuroimaging. *Pediatrics* 2011;127:389–394

DEFINITION OF THE PROBLEM

This practice guideline provides recommendations for the neurodiagnostic evaluation of neurologically healthy infants and children 6 through 60 months of age who have had a simple febrile seizure and present for evaluation within 12 hours of the event. It replaces the 1996 practice parameter. This practice guideline is not intended for patients who have had complex febrile seizures (prolonged, focal, and/or recurrent), and it does not pertain to children with previous neurologic insults, known central nervous system abnormalities, or history of afebrile seizures.

TARGET AUDIENCE AND PRACTICE SETTING

This practice guideline is intended for use by pediatricians, family physicians, child neurologists, neurologists, emergency physicians, nurse practitioners, and other health care providers who evaluate children for febrile seizures.

BACKGROUND

A febrile seizure is a seizure accompanied by fever (temperature ≥ 100.4°F or 38°C2 by any method), without central nervous system infection, that occurs in infants and children 6 through 60 months of age. Febrile seizures occur in 2% to 5% of all children and, as such, make up the most common convulsive event in children younger than 60 months. In 1976, Nelson and Ellenberg,3 using data from the National Collaborative Perinatal Project, further defined febrile seizures as being either simple or complex. Simple febrile seizures were defined as primary generalized seizures that lasted for less than 15 minutes and did not recur within 24 hours. Complex febrile seizures were defined as focal. prolonged (≥15 minutes), and/or recurrent within 24 hours. Children who had simple febrile seizures had no evidence of increased mortality, hemiplegia, or mental retardation. During follow-up evaluation, the risk of epilepsy after a simple febrile seizure was shown to be only slightly higher than that of the general population, whereas the chief risk associated with simple febrile seizures was recurrence in one-third of the children. The authors concluded that simple febrile seizures are benign events with excellent prognoses, a conclusion reaffirmed in the 1980 consensus statement from the National Institutes of Health.^{3,4}

The expected outcomes of this practice guideline include the following:

- Optimize clinician understanding of the scientific basis for the neurodiagnostic evaluation of children with simple febrile seizures.
- 2. Aid the clinician in decision-making by using a structured framework.
- Optimize evaluation of the child who has had a simple febrile seizure by detecting underlying diseases, minimizing morbidity, and reassuring anxious parents and children.
- 4. Reduce the costs of physician and emergency department visits, hospitalizations, and unnecessary testing.
- Educate the clinician to understand that a simple febrile seizure usually does not require further evaluation, specifically electroencephalography, blood studies, or neuroimaging.

METHODOLOGY

To update the clinical practice guideline on the neurodiagnostic evaluation of children with simple febrile seizures,1 the American Academy of Pediatrics (AAP) reconvened the Subcommittee on Febrile Seizures. The committee was chaired by a child neurologist and consisted of a neuroepidemiologist, 3 additional child neurologists, and a practicing pediatrician. All panel members reviewed and signed the AAP voluntary disclosure and conflict-of-interest form. No conflicts were reported. Participation in the guideline process was voluntary and not paid. The guideline was reviewed by members of the AAP Steering Committee on Quality Improvement and Management; members of the AAP Section on Administration and Practice Management, Section on Developmental and Behavioral Pediatrics, Section on Epidemiology, Section on Infectious Diseases, Section on Neurology, Section on Neurologic Surgery, Section on Pediatric Emergency Medicine. Committee on Pediatric Emergency Medicine, Committee on Practice and Ambulatory Medicine, Committee on Child Health Financing, Committee on Infectious Diseases, Committee on Medical Liability and Risk Management, Council on Children With Disabilities, and Council on Community Pediatrics; and members of outside organizations including the Child Neurology Society, the American Academy of Neurology, the American College of Emergency Physicians, and members of the Pediatric Committee of the Emergency Nurses Association.

A comprehensive review of the evidence-based literature published from 1996 to February 2009 was conducted to discover articles that addressed the diagnosis and evaluation of children with simple febrile seizures. Preference was given to population-based studies, but given the scarcity of such studies, data from hospital-based studies, groups of young children with febrile illness, and comparable groups were reviewed. Decisions were made on the basis of a systematic grading of the quality of evidence and strength of recommendations.

In the original practice parameter,¹ 203 medical journal articles were reviewed and abstracted. An additional 372 articles were reviewed and abstracted for this update. Emphasis was placed on articles that differentiated simple febrile seizures from other types of seizures. Tables were constructed from the 70 articles that best fit these criteria.

The evidence-based approach to guideline development requires that the evidence in support of a recommendation be identified, appraised, and summarized and that an explicit link between

Evidence Quality	Preponderance of Benefit or Harm	Balance of Benefit and Harm
A. Well-designed RCTs or diagnostic studies on relevant population	Strong	
B. RCTs or diagnostic studies with minor limitations; overwhelmingly consistent evidence from observational studies		0.11
C. Observational studies (case-control and cohort design)	Rec	Option
D. Expert opinion, case reports, reasoning from first principles	Option	No Rec
X. Exceptional situations for which validating studies cannot be performed and there is a clear preponderance of benefit or harm	Strong Rec	

FIGURE 1

Integrating evidence quality appraisal with an assessment of the anticipated balance between benefits and harms if a policy is carried out leads to designation of a policy as a strong recommendation, recommendation, option, or no recommendation. RCT indicates randomized controlled trial; Rec, recommendation

evidence and recommendations be defined. Evidence-based recommendations reflect the quality of evidence and the balance of benefit and harm that is anticipated when the recommendation is followed. The AAP policy statement "Classifying Recommendations for Clinical Practice Guidelines"5 was followed in designating levels of recommendations (see Fig 1).

KEY ACTION STATEMENTS

Action Statement 1

Action Statement 1a

A lumbar puncture should be performed in any child who presents with a seizure and a fever and has meningeal signs and symptoms (eg, neck stiffness, Kernig and/or Brudzinski signs) or in any child whose history or examination suggests the presence of meningitis or intracranial infection.

- Aggregate evidence level: B (overwhelming evidence from observational studies).
- Benefits: Meningeal signs and symptoms strongly suggest meningitis, which, if bacterial in etiology, will likely be fatal if left untreated.
- Harms/risks/costs: Lumbar puncture is an invasive and often painful procedure and can be costly.

- Benefits/harms assessment: Preponderance of benefit over harm.
- Value judgments: Observational data and clinical principles were used in making this judgment.
- Role of patient preferences: Although parents may not wish to have their child undergo a lumbar puncture, health care providers should explain that if meningitis is not diagnosed and treated, it could be fatal.
- Exclusions: None.
- Intentional vagueness: None.
- Policy level: Strong recommendation.

Action Statement 1b

In any infant between 6 and 12 months of age who presents with a seizure and fever, a lumbar puncture is an option when the child is considered deficient in Haemophilus influenzae type b (Hib) or Streptococcus pneumoniae immunizations (ie, has not received scheduled immunizations as recommended) or when immunization status cannot be determined because of an increased risk of bacterial meningitis.

- Aggregate evidence level: D (expert opinion, case reports).
- Benefits: Meningeal signs and symptoms strongly suggest meningitis. which, if bacterial in etiology, will

- likely be fatal or cause significant long-term disability if left untreated.
- Harms/risks/costs: Lumbar puncture is an invasive and often painful procedure and can be costly.
- Benefits/harms assessment: Preponderance of benefit over harm.
- Value judgments: Data on the incidence of bacterial meningitis from before and after the existence of immunizations against Hib and S pneumoniae were used in making this recommendation.
- Role of patient preferences: Although parents may not wish their child to undergo a lumbar puncture, health care providers should explain that in the absence of complete immunizations, their child may be at risk of having fatal bacterial meningitis.
- Exclusions: This recommendation applies only to children 6 to 12 months of age. The subcommittee felt that clinicians would recognize symptoms of meningitis in children older than 12 months.
- Intentional vagueness: None.
- Policy level: Option.

Action Statement 1c

A lumbar puncture is an option in the child who presents with a seizure and fever and is pretreated with antibiotics, because antibiotic treatment can mask the signs and symptoms of meningitis.

- Aggregate evidence level: D (reasoning from clinical experience, case series).
- Benefits: Antibiotics may mask meningeal signs and symptoms but may be insufficient to eradicate meningitis; a diagnosis of meningitis, if bacterial in etiology, will likely be fatal if left untreated.
- Harms/risks/costs: Lumbar puncture is an invasive and often painful procedure and can be costly.

- Benefits/harms assessment: Preponderance of benefit over harm.
- Value judgments: Clinical experience and case series were used in making this judgment while recognizing that extensive data from studies are lacking.
- Role of patient preferences: Although parents may not wish to have their child undergo a lumbar puncture, medical providers should explain that in the presence of pretreatment with antibiotics, the signs and symptoms of meningitis may be masked. Meningitis, if untreated, can be fatal.
- Exclusions: None.
- Intentional vagueness: Data are insufficient to define the specific treatment duration necessary to mask signs and symptoms. The committee determined that the decision to perform a lumbar puncture will depend on the type and duration of antibiotics administered before the seizure and should be left to the individual clinician.
- Policy level: Option.

The committee recognizes the diversity of past and present opinions regarding the need for lumbar punctures in children younger than 12 months with a simple febrile seizure. Since the publication of the previous practice parameter,1 however, there has been widespread immunization in the United States for 2 of the most common causes of bacterial meningitis in this age range: Hib and Spneumoniae. Although compliance with all scheduled immunizations as recommended does not completely eliminate the possibility of bacterial meningitis from the differential diagnosis, current data no longer support routine lumbar puncture in well-appearing, fully immunized children who present with a simple febrile seizure.6-8 Moreover, although approximately 25% of young children with meningitis have seizures as the presenting sign of the disease, some are either obtunded or comatose when evaluated by a physician for the seizure, and the remainder most often have obvious clinical signs of meningitis (focal seizures, recurrent seizures, petechial rash, or nuchal rigidity).9-11 Once a decision has been made to perform a lumbar puncture, then blood culture and serum glucose testing should be performed concurrently to increase the sensitivity for detecting bacteria and to determine if there is hypoglycorrhachia characteristic of bacterial meningitis, respectively. Recent studies that evaluated the outcome of children with simple febrile seizures have included populations with a high prevalence of immunization.^{7,8} Data for unimmunized or partially immunized children are lacking. Therefore, lumbar puncture is an option for young children who are considered deficient in immunizations or those in whom immunization status cannot be determined. There are also no definitive data on the outcome of children who present with a simple febrile seizure while already on antibiotics. The authors were unable to find a definition of "pretreated" in the literature, so they consulted with the AAP Committee on Infectious Diseases. Although there is no formal definition, pretreatment can be considered to include systemic antibiotic therapy by any route given within the days before the seizure. Whether pretreatment will affect the presentation and course of bacterial meningitis cannot be predicted but will depend, in part, on the antibiotic administered, the dose, the route of administration, the drug's cerebrospinal fluid penetration, and the organism causing the meningitis. Lumbar puncture is an option in any child pretreated with antibiotics before a simple febrile seizure.

Action Statement 2

An electroencephalogram (EEG) should not be performed in the evaluation of a neurologically healthy child with a simple febrile seizure.

- Aggregate evidence level: B (overwhelming evidence from observational studies).
- Benefits: One study showed a possible association with paroxysmal EEGs and a higher rate of afebrile seizures.¹²
- Harms/risks/costs: EEGs are costly and may increase parental anxiety.
- Benefits/harmsassessment: Preponderance of harm over benefit.
- Value judgments: Observational data were used for this judgment.
- Role of patient preferences: Although an EEG might have limited prognostic utility in this situation, parents should be educated that the study will not alter outcome.
- Exclusions: None.
- Intentional vagueness: None.
- Policy level: Strong recommendation.

There is no evidence that EEG readings performed either at the time of presentation after a simple febrile seizure or within the following month are predictive of either recurrence of febrile seizures or the development of afebrile seizures/epilepsy within the next 2 years. ^{13,14} There is a single study that found that a paroxysmal EEG was associated with a higher rate of afebrile seizures. ¹² There is no evidence that interventions based on this test would alter outcome.

Action Statement 3

The following tests should not be performed routinely for the sole purpose of identifying the cause of a simple febrile seizure: measurement of serum electrolytes, calcium, phosphorus, magnesium, or blood glucose or complete blood cell count.

- Aggregate evidence level: B (overwhelming evidence from observational studies).
- Benefits: A complete blood cell count may identify children at risk for bacte-

remia; however, the incidence of bacteremia in febrile children younger than 24 months is the same with or without febrile seizures.

- Harms/risks/costs: Laboratory tests may be invasive and costly and provide no real benefit.
- Benefits/harmsassessment: Preponderance of harm over benefit.
- Value judgments: Observational data were used for this judgment.
- Role of patient preferences: Although parents may want blood tests performed to explain the seizure, they should be reassured that blood tests should be directed toward identifying the source of their child's fever.
- Exclusions: None.
- Intentional vagueness: None.
- Policy level: Strong recommendation.

There is no evidence to suggest that routine blood studies are of benefit in the evaluation of the child with a simple febrile seizure. 15-18 Although some children with febrile seizures have abnormal serum electrolyte values, their condition should be identifiable by obtaining appropriate histories and performing careful physical examinations. It should be noted that as a group, children with febrile seizures have relatively low serum sodium concentrations. As such, physicians and caregivers should avoid overhydration with hypotonic fluids. 18 Complete blood cell counts may be useful as a means of identifying young children at risk of bacteremia. It should be noted, however, that the incidence of bacteremia in children younger than 24 months with or without febrile seizures is the same. When fever is present, the decision regarding the need for laboratory testing should be directed toward identifying the source of the fever rather than as part of the routine evaluation of the seizure itself.

Action Statement 4

Neuroimaging should not be performed in the routine evaluation of the child with a simple febrile seizure.

- Aggregate evidence level: B (overwhelming evidence from observational studies).
- Benefits: Neuroimaging might provide earlier detection of fixed structural lesions, such as dysplasia, or very rarely, abscess or tumor.
- Harms/risks/costs: Neuroimaging tests are costly, computed tomography (CT) exposes children to radiation, and MRI may require sedation.
- Benefits/harmsassessment: Preponderance of harm over benefit.
- Value judgments: Observational data were used for this judgment.
- Role of patient preferences: Although parents may want neuroimaging performed to explain the seizure, they should be reassured that the tests carry risks and will not alter outcome for their child.
- Exclusions: None.
- Intentional vagueness: None.
- Policy level: Strong recommendation.

The literature does not support the use of skull films in evaluation of the child with a febrile seizure. 15,19 No data have been published that either support or negate the need for CT or MRI in the evaluation of children with simple febrile seizures. Data, however, show that CT scanning is associated with radiation exposure that may escalate future cancer risk. MRI is associated with risks from required sedation and high cost. 20,21 Extrapolation of data from the

literature on the use of CT in neurologically healthy children who have generalized epilepsy has shown that clinically important intracranial structural abnormalities in this patient population are uncommon.^{22,23}

CONCLUSIONS

Clinicians evaluating infants or young children after a simple febrile seizure should direct their attention toward identifying the cause of the child's fever. Meningitis should be considered in the differential diagnosis for any febrile child, and lumbar puncture should be performed if the child is illappearing or if there are clinical signs or symptoms of concern. A lumbar puncture is an option in a child 6 to 12 months of age who is deficient in Hib and S pneumoniae immunizations or for whom immunization status is unknown. A lumbar puncture is an option in children who have been pretreated with antibiotics. In general, a simple febrile seizure does not usually reguire further evaluation, specifically EEGs, blood studies, or neuroimaging.

SUBCOMMITTEE ON FEBRILE SEIZURES, 2002–2010

Patricia K. Duffner, MD (neurology, no conflicts)

Peter H. Berman, MD (neurology, no conflicts)
Robert J. Baumann, MD (neuroepidemiology,
no conflicts)

Paul Graham Fisher, MD (neurology, no conflicts)

John L. Green, MD (general pediatrics, no conflicts)

Sanford Schneider, MD (neurology, no conflicts)

STAFF

Caryn Davidson, MA

OVERSIGHT BY THE STEERING COMMITTEE ON QUALITY IMPROVEMENT AND MANAGEMENT, 2009-2011

REFERENCES

- 1. American Academy of Pediatrics, Provisional Committee on Quality Improvement and Subcommittee on Febrile Seizures. Practice parameter: the neurodiagnostic evaluation of a child with a first simple febrile seizure. Pediatrics. 1996;97(5): 769-772; discussion 773-775
- 2. Michael Marcy S, Kohl KS, Dagan R, et al; Brighton Collaboration Fever Working Group. Fever as an adverse event following immunization: case definition and guidelines of data collection, analysis, and presentation. Vaccine. 2004;22(5-6):551-556
- 3. Nelson KB, Ellenberg JH. Predictors of epilepsy in children who have experienced febrile seizures. N Engl J Med. 1976;295(19): 1029 - 1033
- 4. Consensus statement: febrile seizureslong-term management of children with fever-associated seizures. Pediatrics. 1980; 66(6):1009-1012
- 5. American Academy of Pediatrics, Steering Committee on Quality Improvement and Management. Classifying recommendations for clinical practice guidelines. Pediatrics. 2004;114(3):874-877
- 6. Trainor JL, Hampers LC, Krug SE, Listernick R. Children with first-time simple febrile seizures are at low risk of serious bacterial illness. Acad Emera Med. 2001:8(8):781-787
- 7. Shaked 0, Peña BM, Linares MY, Baker RL. Simple febrile seizures: are the AAP guidelines regarding lumbar puncture being followed? Pediatr Emerg Care. 2009;25(1):
- 8. Kimia AA, Capraro AJ, Hummel D, Johnston

- P, Harper MB. Utility of lumbar puncture for first simple febrile seizure among children 6 to 18 months of age. Pediatrics. 2009; 123(1):6-12
- 9. Warden CR, Zibulewsky J, Mace S, Gold C, Gausche-Hill M. Evaluation and management of febrile seizures in the out-ofhospital and emergency department settings. Ann Emerg Med. 2003;41(2):215-222
- 10. Rutter N, Smales OR. Role of routine investigations in children presenting with their first febrile convulsion. Arch Dis Child. 1977; 52(3):188-191
- 11. Green SM, Rothrock SG, Clem KJ, Zurcher RF, Mellick L. Can seizures be the sole manifestation of meningitis in febrile children? Pediatrics. 1993;92(4):527-534
- 12. Kuturec M, Emoto SE, Sofijanov N, et al. Febrile seizures: is the EEG a useful predictor of recurrences? Clin Pediatr (Phila), 1997: 36(1):31-36
- 13. Frantzen E, Lennox-Buchthal M, Nygaard A. Longitudinal EEG and clinical study of children with febrile convulsions. Electroencephalogr Clin Neurophysiol. 1968;24(3): 197-212
- 14. Thorn I. The significance of electroencephalography in febrile convulsions. In: Akimoto H, Kazamatsuri H, Seino M, Ward A, eds. Advances in Epileptology: XIIIth International Epilepsy Symposium. New York, NY: Raven Press: 1982:93-95
- 15. Jaffe M, Bar-Joseph G, Tirosh E. Fever and convulsions: indications for laboratory investigations. Pediatrics. 1981;67(5): 729 - 731

- 16. Gerber MA, Berliner BC. The child with a "simple" febrile seizure: appropriate diagnostic evaluation. Am J Dis Child. 1981; 135(5):431-443
- 17. Heijbel J, Blom S, Bergfors PG. Simple febrile convulsions: a prospective incidence study and an evaluation of investigations initially needed. Neuropadiatrie. 1980;11(1): 45-56
- 18. Thoman JE, Duffner PK, Shucard JL. Do serum sodium levels predict febrile seizure recurrence within 24 hours? Pediatr Neurol. 2004;31(5):342-344
- 19. Nealis GT, McFadden SW, Ames RA, Ouellette EM. Routine skull roentgenograms in the management of simple febrile seizures. JPediatr. 1977;90(4):595-596
- 20. Stein SC, Hurst RW, Sonnad SS. Metaanalysis of cranial CT scans in children: a mathematical model to predict radiationinduced tumors associated with radiation exposure that may escalate future cancer risk. Pediatr Neurosurg. 2008;44(6): 448 - 457
- 21. Brenner DJ, Hall EJ. Computed tomography: an increasing source of radiation exposure. N Engl J Med. 2007;357(22):2277-2284
- 22. Yang PJ, Berger PE, Cohen ME, Duffner PK. Computed tomography and childhood seizure disorders. Neurology. 1979;29(8): 1084 - 1088
- 23. Bachman DS, Hodges FJ, Freeman JM. Computerized axial tomography in chronic seizure disorders of childhood. Pediatrics. 1976;58(6):828-832

Febrile Seizures: Guideline for the Neurodiagnostic Evaluation of the Child With a Simple Febrile Seizure

Subcommittee on Febrile Seizures

Pediatrics 2011;127;389

DOI: 10.1542/peds.2010-3318

Updated Information & including high resolution figures, can be found at:

Services http://pediatrics.aappublications.org/content/127/2/389.full.ht

ml

References This article cites 22 articles, 11 of which can be accessed free

at:

http://pediatrics.aappublications.org/content/127/2/389.full.ht

ml#ref-list-1

Citations This article has been cited by 3 HighWire-hosted articles:

http://pediatrics.aappublications.org/content/127/2/389.full.ht

ml#related-urls

Post-Publication 3 P³Rs have been posted to this article

Peer Reviews (P³Rs) http://pediatrics.aappublications.org/cgi/eletters/127/2/389

Permissions & Licensing Information about reproducing this article in parts (figures,

tables) or in its entirety can be found online at:

http://pediatrics.aappublications.org/site/misc/Permissions.xht

Reprints Information about ordering reprints can be found online:

http://pediatrics.aappublications.org/site/misc/reprints.xhtml

PEDIATRICS is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. PEDIATRICS is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2011 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0031-4005. Online ISSN: 1098-4275.

