Evaluation and Treatment of the Child with Febrile Seizure

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Up to 5 percent of children in North America and western Europe experience at least one episode of febrile seizure before six years of age. Most of these seizures are self-limited and patients do not require treatment. Continuous therapy after the seizure is not effective in reducing the development of afebrile seizures. Antipyretics are effective in reducing the risk of febrile seizures if given early in the illness. Immediate care for the patient who has had a febrile seizure includes stopping the seizure, if prolonged, and evaluating the patient for the cause of the fever. Bacterial infections are treatable sources of fever but are not usually the cause of the fever that triggers a seizure. The patient must be assessed for these treatable sources. Long-term consequences of febrile seizure are rare in children who are otherwise healthy. Current recommendations do not support the use of continuing or intermittent neuroleptic or benzodiazepine suppressive therapies after a simple febrile seizure. (Am Fam Physician 2006;73:1761-4, 1765-6. Copyright © 2006 American Academy of Family Physicians.)

▶ **Patient information:** A handout on febrile seizure, adapted from the National Institutes of Health Web site, is provided on page 1765.

Febrile seizures are common, with 2 to 5 percent of children in North America experiencing at least one; the majority (65 to 90 percent) of these are simple febrile seizures. Children with febrile seizures are usually six months to five years of age; the peak occurrence is in children 18 to 24 months of age. The 1993 International League Against Epilepsy defined a febrile seizure as "an epileptic seizure occurring in childhood associated with fever, but without evidence of intracranial infection or defined cause. Seizures with fever in children who have experienced a previous nonfebrile seizure are excluded."[1] The clinical evaluation process is based on the nature of the febrile seizure and the underlying illness that triggered the initial fever. Febrile seizures are broadly defined as simple or complex *(Table 1[2])*.[3]

TABLE 1
Simple vs. Complex Febrile Seizures

Simple febrile seizure	*Complex febrile seizure*
Lasts less than 15 minutes	Lasts 15 minutes or longer
Occurs once in a 24-hour period	Occurs more than once in a 24-hour period
Generalized	Focal
No previous neurologic problems	Patient has known neurologic problems, such as cerebral palsy

Information from reference 2.

Risk Factors

The primary risk factors for a first febrile seizure are day care center attendance, developmental delay, having a first- or second-degree relative with a history of febrile seizure, and a neonatal nursery stay of more than 30 days.[4] Case-control studies[5] have found the male to female ratio to be 1.4:1. Children with any two of the four risk factors have a 28 percent chance of experiencing at least one febrile seizure. For children with a febrile illness, the prime risk factors are the height of the fever and a family history of febrile seizures. Specifically, 10 percent of siblings and 10 percent of offspring of a person who had a childhood febrile seizure also will have seizures with fever.[5] In one study,[6] mean ferritin levels were lower in children who had a seizure with fever, suggesting a possible factor in febrile seizures.

The risk factors for recurrent seizures are provided in *Table 2*.[4] Ethnicity, sex, neurodevelopmental abnormality, and a complex febrile seizure with one or more complex features are not risk factors for the recurrence of febrile seizures. The risk factors for the development of afebrile seizures

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	Evidence rating	References
Because intensive routine use of antipyretic agents does not reduce the incidence of recurrent febrile seizures in children, parents can be instructed in the intermittent use of antipyretic agents with febrile illnesses.	B	3, 18
Neuroleptics should not be used for the long term because they do not reduce the risk of epilepsy after a febrile seizure and are potentially toxic.	B	2, 20
Neuroimaging and electroencephalography are not indicated routinely after a single episode of simple febrile seizure.	C	1, 18, 19

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, see page 1687 or http://www.aafp.org/afpsort.xml.

(i.e., epilepsy) after an episode of febrile seizure are listed in *Table 3*.[4] In one study,[5] investigators found that 10 percent of children with febrile seizures subsequently developed an afebrile seizure disorder.

Ethnicity, sex, family history of febrile seizures, age at first febrile seizure, and height of fever are not risk factors for the subsequent development of epilepsy. Investigators in a 12-year study[7] found no association between mesial temporal sclerosis and single or complex seizures with fever. Mesial temporal sclerosis is the most common lesion found in patients with temporal lobe epilepsy. The presence or absence of the above-mentioned risk factors is important for reassuring the parents, identifying patients who might warrant additional evaluation, and assessing the patient who has experienced a repeat seizure with fever.

Evaluation

The acute component of the evaluation of the febrile child with a seizure is the same as for any child with a fever.[1,8-11] Measures include clinical history, presence of chronic illness, recent antibiotic therapy, recent immunizations,[12] and day care attendance. As many as 10 percent of infants younger than three months who appear to be well and have a temperature above 100.4°F (38°C) have a serious bacterial infection or meningitis. Two percent of infants and children older than three months with a temperature above 102.2°F (39°C) are found to have bacteremia.

The authors of one retrospective study[13] in children presenting with a febrile seizure examined the incidence of bacterial infections, including unsuspected meningitis. Bacteremia with *Streptococcus pneumoniae* was noted in 3 percent of the patients, urinary tract infection in 1 percent, and none of the patients had bacterial meningitis. Children with more than 8 white blood cells per mL of cerebral spinal fluid, known seizure disorder or other chronic neurologic disorder, or who had a documented immunodeficiency were excluded from the study.

In another retrospective study[14] focusing on only simple febrile seizures, investigators found a 1.3 percent incidence of bacteremia with *S. pneumoniae*, a 6 percent incidence of urinary tract infection, and no meningitis. Patients who were unarousable or comatose after seizure were excluded from the study, which may account for the low incidence of meningitis. Streptococcal bacteremia and meningitis will become less common as the prevalence of immunization increases.

Current recommendations include consideration of a lumbar puncture, especially in children younger than 18 months, because meningeal signs are less reliable

TABLE 2
Risk Factors for Recurrent Febrile Seizures

Younger than 18 months
Duration of fever (i.e., shorter duration of fever before seizure equals higher risk of recurrence)
Family history of epilepsy (possible, not definitive)
Family history of febrile seizures
Height of fever (i.e., the lower the peak fever, the higher the rate of recurrence)

Adapted with permission from Shinnar S, Glauser TA. Febrile seizures. J Child Neurol 2002;17(suppl 1):S45.

TABLE 3
Risk Factors for the Development of Afebrile Seizures After an Episode of Febrile Seizure

Complex febrile seizure*
Duration of fever (i.e., one hour or less equals increased risk)
Family history of epilepsy
Neurodevelopmental abnormality (e.g., cerebral palsy, hydrocephalus)

**—A possible risk factor is more than one complex feature of the febrile seizure.*

Adapted with permission from Shinnar S, Glauser TA. Febrile seizures. J Child Neurol 2002;17(suppl 1):S46.

in this group.[15] The prevalence of meningitis among patients with a febrile seizure was 1 to 2 percent, and the absence of any remarkable findings on the history or physical examination makes bacterial meningitis unlikely as the cause of the fever and seizure.[16] Other laboratory studies,[1,17] such as measurement of serum electrolyte levels, are most beneficial in situations with clear symptoms or signs of a concurrent illness, such as diarrhea or vomiting.

Neuroimaging (i.e., cranial magnetic resonance imaging [MRI] or computed tomography) is indicated in the child with a febrile seizure and evidence of increased intracranial pressure, history or examination suggestive of trauma, or a possible structural defect (in cases of microcephaly or spasticity).[1,18] If a neuroimaging study is obtained, MRI is the preferred modality.[19] Results of prospective studies[2,18] have not found electroencephalography to be helpful in predicting the likelihood of developing afebrile seizure disorders later in life. Consultation with a neurology subspecialist rarely is needed for the child with a febrile seizure, especially a simple febrile seizure.

Treatment

Current guidelines[2,3,20] do not recommend the use of continuous or intermittent therapy with neuroleptics or benzodiazepines after a simple febrile seizure. No medication has been shown to reduce the risk of an afebrile seizure (i.e., epilepsy) after a simple febrile seizure. Intense routine use of antipyretic agents has been no more effective in reducing the incidence of recurrent febrile seizures than the intermittent use of the antipyretic agents when a febrile episode is noted.[18] Although valproic acid (Depakene), diazepam (Valium), lorazepam (Ativan), and fosphenytoin (Cerebyx) are indicated for the management of seizures, they have not been indicated explicitly for the management of febrile seizures.

The use of phenobarbital (5 to 8 mg per kg of weight per day for children two to 24 months of age, and 3 to 5 mg per kg per day for children older than two years) and valproic acid (10 to 15 mg per kg per day in divided doses, with a maximal dosage of 60 mg per kg per day) on a continuous basis reduces the risk of recurrent febrile seizures but has significant side effects. Phenobarbital is associated with transient sleep disturbances, decreased memory, and reduced concentration. Valproic acid therapy is associated with hematopoietic disruptions, renal toxicity, pancreatitis, and fatal hepatotoxicity.

The use of intermittent oral diazepam also has been found to reduce the risk of recurrent febrile seizures, but the effectiveness is limited. In one randomized controlled trial,[3] recurrence was noted in 15 percent of patients receiving diazepam and 18 percent of patients receiving placebo. One reason for this limited effectiveness was that nearly one half of patients in the oral diazepam and placebo groups experienced febrile seizure as the first sign of a febrile illness. Hyperactivity was the most common side effect in the oral diazepam group, and other side effects included lethargy, ataxia, and drowsiness. Concern has been expressed that the latter side effects could mask an evolving infection of the central nervous system.

For patients who have an ongoing seizure at the time of assessment (i.e., febrile status epilepticus), intravenous diazepam (0.2 to 0.5 mg per kg of weight intravenously every 15 minutes for a cumulative dosage of 5 mg in children one month to five years of age) often is effective. For the pre-hospital treatment of a seizure or for patients in whom intravenous access is limited, rectal diazepam (a single dose of 0.5 mg per kg for children two to five years of age) or diazepam gel is an option.[4] Lorazepam (0.1 mg

per kg up to 4 mg) is another intravenous medication, and it has a longer duration of action compared with diazepam.

Finally, if the seizure continues after an adequate dose of diazepam (or other benzodiazepine) is administered, a full status epilepticus treatment protocol is indicated.[21] Fosphenytoin has several theoretic and clinical advantages compared with phenytoin (Dilantin): a more convenient, rapid route of intravenous administration; the ability to reach therapeutic levels more quickly; the availability for intramuscular injection; and a relatively low potential for adverse local reactions at injection sites. If this additional measure is not successful, intubation and anesthesia are the recommended final measures.

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REFERENCES

1. Rosman NP. Evaluation of the child who convulses with fever. Paediatr Drugs 2003;5:457-61.
2. Practice parameter: long-term treatment of the child with simple febrile seizures. American Academy of Pediatrics. Committee on Quality Improvement, Subcommittee on Febrile Seizures. Pediatrics 1999;103 (6 pt 1):1307-9.
3. Baumann RJ. Technical report: treatment of the child with simple febrile seizures. Pediatrics 1999;103:e86.
4. Shinnar S, Glauser TA. Febrile seizures. J Child Neurol 2002;17(suppl 1):S44-52.
5. Pal DK, Kugler SL, Mandelbaum DE, Durner M. Phenotypic features of familial febrile seizures: case-control study. Neurology 2003;60:410-4.
6. Daoud AS, Batieha A, Abu-Ekteish F, Gharaibeh N, Ajlouni S, Hijazi S. Iron status: a possible risk factor for the first febrile seizure. Epilepsia 2002;43:740-3.
7. Tarkka R, Paakko E, Pyhtinen J, Uhari M, Rantala H. Febrile seizures and mesial temporal sclerosis: no association in a long-term follow-up study. Neurology 2003;60:215-8.
8. Luszczak M. Evaluation and management of infants and young children with fever. Am Fam Physician 2001;64:1219-26.
9. Warden CR, Zibulewsky J, Mace S, Gold C, Gausche-Hill M. Evaluation and management of febrile seizures in the out-of-hospital and emergency department settings. Ann Emerg Med 2003;41:215-22.
10. Shah SS, Alpern ER, Zwerling L, Reid JR, McGowan KL, Bell LM. Low risk of bacteremia in children with febrile seizures. Arch Pediatr Adolesc Med 2002;156:469-72.
11. Pantell RH, Newman TB, Bernzweig J, Bergman DA, Takayama JI, Segal M, et al. Management and outcomes of care of fever in early infancy. JAMA 2004;291:1203-12.
12. Vestergaard M, Hviid A, Madsen KM, Wohlfahrt J, Thorsen P, Schendel D, et al. MMR vaccination and febrile seizures: evaluation of susceptible subgroups and long-term prognosis. JAMA 2004;292:351-7.
13. Teach SJ, Geil PA. Incidence of bacteremia, urinary tract infections, and unsuspected bacterial meningitis in children with febrile seizures. Pediatr Emerg Care 1999;15:9-12.
14. Trainor JL, Hampers LC, Krug SE, Listernick R. Children with first-time simple febrile seizures are at low risk of serious bacterial illness. Acad Emerg Med 2001;8:781-7.
15. McAbee GN, Wark JE. A practical approach to uncomplicated seizures in children. Am Fam Physician 2000; 62:1109-16.
16. Offringa M, Moyer VA. An evidence-based approach to managing seizures associated with fever in children. West J Med 2001;175:254-9.
17. Uemura N, Okumura A, Negoro T, Watanabe K. Clinical features of benign convulsions with mild gastroenteritis. Brain Dev 2002;24:745-9.
18. Chadwick DJ 2nd. Febrile seizures: an overview. Minn Med 2003;86:41-3.
19. Hirtz D, Ashwal S, Berg A, Bettis D, Camfield C, Camfield P, et al. Practice parameter: evaluating a first nonfebrile seizure in children: report of the quality standards subcommittee of the American Academy of Neurology, The Child Neurology Society, and The American Epilepsy Society. Neurology 2000;55:616-23.
20. Hirtz D, Berg A, Bettis D, Camfield C, Camfield P, Crumrine P, et al. Practice parameter: treatment of the child with a first unprovoked seizure: report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. Neurology 2003;60:166-75.
21. Appleton R, Choonara I, Martland T, Phillips B, Scott R, Whitehouse W. The treatment of convulsive status epilepticus in children. The Status Epilepticus Working Party, Members of the Status Epilepticus Working Party. Arch Dis Child 2000;83:415-9.