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Evaluation and management of febrile seizures in the out-of-hospital and emergency department settings

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Febrile seizures are the most common seizures seen in children younger than 5 years old. Out-of-hospital and emergency department providers need to be familiar with

the principles of the evaluation and management of this common disorder. Most febrile seizures are brief, do not require any specific treatment or extensive workup, and have a benign prognosis. Recognizing the pattern of a simple febrile seizure in young children is important to limit interventions and to reassure parents. Patients with febrile seizures are not at higher risk for serious bacterial illnesses than similarly aged febrile patients. Excluding meningitis and encephalitis are the primary clinical interventions through a thorough history and physical examination and, occasionally, a lumbar puncture. Reassuring parents of patients with febrile seizures and arranging primary care follow-up are important roles for the emergency physician. [Ann Emerg Med. 2003;41:215–222.]

Introduction

Febrile seizures are the most common seizures seen in the pediatric population in the out-of-hospital and emergency department settings, and they account for the majority of seizures seen in children younger than 5 years old.^{[1] [2]} Therefore, it is important for out-of-hospital and ED personnel to be familiar with the principles of their evaluation and management. This article will not address patients with previous afebrile seizures, known central nervous system abnormalities, or seizures caused by head trauma, encephalitis, meningitis, or toxic exposure. This article is a collective review representing a thorough search of the literature without a strict rating of the quality of cited articles.

A febrile seizure is any seizure occurring in an infant or young child (6 months to 5 years old) in conjunction with a fever (temperature $>38^{\circ}\text{C}$ [100.4°F]) or history of recent fever and without evidence of a previous afebrile seizure or an underlying cause, such as neurologic disease or central nervous system (CNS) infection.^[3] These can be classified as simple or complex. A simple febrile seizure lasts less than 15 minutes, is initially generalized in nature, and occurs only once during a 24-hour period.^[3] A complex febrile seizure is differentiated from a simple febrile seizure by lasting greater than 15 minutes, having focal features at any time, or recurring within a 24-hour period.^[3] The majority of febrile seizures last less than several minutes.^[4] Lastly, a fever and seizure is any seizure that occurs concurrently with a fever, including simple febrile seizures and complex febrile seizures, but that also might occur in patients with an underlying seizure disorder, patients out of the febrile seizure age range, or patients having evidence of a CNS infection. Because fevers are very common and seizures relatively common in this age group, it is not infrequent that the presence of fever might be unrelated to the cause of the seizure.

Epidemiology

Febrile seizures occur at some point in 2% to 4% of children worldwide.^[5] There are no geographic, racial, or ethnic differences in incidence.

There is a history of febrile seizures in immediate family members in 25% to 40% of cases. Offspring of a parent with a history of febrile seizures have 4.4 times the risk of

the general population; the risk increases to 20 times if both parents have histories of febrile seizures. Siblings of a patient with febrile seizures have 3.6 times the risk of the general population. The concordance rate in monozygotic twins is much higher than that in dizygotic twins. Even second-degree relatives (eg, nieces, nephews) have 2.7 times the risk of the general population.^[4]

Viral infections are frequently associated with febrile seizures.^{[6] [7]} In one study, a viral cause was identified in 47% of patients with first-time febrile seizures, with human herpesvirus 6 (the most common causative agent of roseola) being cultured in 19% and convalescent titers for herpes simplex virus increasing in 26% of patients with a documented cause.^[8] Human herpesvirus 7 and influenza A and B were also found to be important causes. The rates of serious bacterial infections in patients with febrile seizures are equivalent to those in age-matched febrile control patients without seizures, as demonstrated in 2 comprehensive studies.^{[9] [10]} There is also a significant increased risk of febrile seizures on the day of vaccination with diphtheria and tetanus toxoids and whole-cell pertussis vaccine and in 8 to 14 days after a measles, mumps, and rubella vaccination, but these are not associated with any long-term adverse consequences.^[11]

Febrile seizures frequently recur with subsequent febrile illnesses, and several studies have examined recurrence risk factors. Knudsen^[12] evaluated recurrence risk factors for febrile seizures in an 18-month postseizure follow-up study. He demonstrated the following as significant risk factors: (1) age of 15 months or younger at onset; (2) history of epilepsy or febrile seizures in first-degree relatives; (3) many episodes of fever; or (4) an initial complex febrile seizure. The rates of recurrence were 10% in patients with no risk factors, 25% to 50% for those with 1 or 2 risk factors, and 50% to 100% for those with 3 or more risk factors.

A meta-analysis by Offringa et al^[13] of 5 studies found that the following factors were associated with an increased risk of a child having a complex febrile seizure: (1) age younger than 12 months at onset; (2) a history of febrile or afebrile seizures in first-degree relatives; and (3) a lower rectal temperature (<40°C [$<104^{\circ}\text{F}$]) during the initial seizure. A second meta-analysis of 14 studies by Berg et al^[14] showed that high risk factors for febrile seizure recurrence were as follows: Age of 12 months or less at onset or family history of febrile seizures each carried a recurrence risk of 50%. Berg et al did not find a consistent increased risk for patients with a family history of afebrile seizures and only found a small increase in risk for patients with focal, prolonged, or multiple seizures.

Berg et al,^[15] in a different study, prospectively evaluated 347 children aged 1 month to 10 years for risk of recurrence. Of these children, 94 (27%) had recurrent febrile seizures, with a recurrence risk of 25% at 1 year and 30% at 2 years. The recurrence rate increased with decreased duration of fever with the first febrile seizure, age younger than 18 months (30% versus 18%), and family history of febrile seizure (36% versus 20%). In this study, the level of fever with first febrile seizure was inversely related to risk of recurrence (35% risk at a temperature of 38.3°C [100.9°F] and 13% risk at a temperature of 40.6°C [105.1°F]). The duration of fever before the initial seizure was associated with

the risk of recurrence at 1 year: For fever lasting less than 1 hour, the risk of recurrence was 44%; for fever lasting 1 to 24 hours, the risk of recurrence was 23%; and for fever lasting more than 24 hours, the risk of recurrence was 13% ($P < .001$). In this study, complex features of seizure, family history of epilepsy, or previous neurologic abnormality did not increase rate of recurrence.

Overall, the risk of recurrent febrile seizures is increased in younger patients with a first-time febrile seizure (<12 months old), patients with lower temperatures on presentation of their first seizure (<40°C), patients with shorter duration of fever before the seizure (<24 hours), patients with a family history of febrile seizures, and, less consistently, patients having complex features with the first febrile seizure. This information is important for the emergency physician to provide anticipatory guidance to the family (Figure).

- Febrile seizures occur in 2% to 5% of all children between the ages of 6 months and 5 years.
- These seizures might appear frightening to observers but are generally harmless.
- Simple febrile seizures often occur in the first 24 hours of the febrile illness and only occur once. If the seizure recurs, your child should be reevaluated.
- A febrile seizure might be manifested by body stiffening; twitching of the face, arms and legs, or both; eye rolling; jerking of the arms and legs; staring; or loss of consciousness. Febrile seizures generally last <1 minute but can last up to 15 minutes.
- Your child might appear not to be breathing, and the skin color might become darker. If so, call 911 or emergency personnel and lay the child on the floor on his or her back and DO NOT place your fingers in the child's mouth.
- Febrile seizures do not cause brain damage or paralysis.
- A child who has febrile seizures has only a slightly increased risk of having a seizure disorder compared with that of a child who has never had a febrile seizure.
- Febrile seizures tend to run in families.
- Febrile seizures can recur with subsequent febrile illnesses. Medicines are generally not given to prevent simple febrile seizures.
- Use of medicines such as acetaminophen or ibuprofen for fevers have not been shown to prevent febrile seizures.

Figure. Advice to parents about simple febrile seizures.

In the general population, the risk of development of epilepsy by age 7 years is approximately 1%.^[5] Children having had one simple febrile seizure have a slightly higher risk of developing epilepsy. Children who were younger than 12 months old when they had their first simple febrile seizure or those having had multiple simple febrile seizures

have a 2.4% risk of developing epilepsy.^[16] In contrast, the risk of development of epilepsy increases to 30 to 50 times that of the general population in patients with one or more complex febrile seizures, particularly seizures with focal features in a child with abnormal neurologic development. There is no evidence that treating children who have had a simple febrile seizure with seizure prophylaxis, such as diazepam, prevents future epilepsy.^[17] There is also no evidence that children with simple febrile seizures have any difference in cognitive outcomes than children without simple febrile seizures.^[18]

Out-of-hospital evaluation and management

Patients with febrile seizures are frequently encountered by emergency medical services providers.^[2] The majority of these patients will not be actively seizing on arrival of emergency medical services providers and will generally only require supportive care and transport to an ED. The initial evaluation of these patients should include assessment of the patient's airway patency, ventilation and oxygenation adequacy, and circulatory status. Routine care should include oxygen administration as necessary by mask, nasal cannula, or oxygen tubing to maintain adequate oxygenation; cardiac monitoring and pulse oximetry; and assessment of the need for intravenous access in patients with persistent or recurrent seizures. Initial airway and ventilation maneuvers usually will be noninvasive because it is likely that the patient's airway status will improve as the postictal state, the effect of medications (if administered), or both resolve. Bag-mask ventilation might be needed for patients who do not respond to these maneuvers or patients in respiratory arrest. Definitive airway adjuncts, such as endotracheal intubation, are rarely needed in the out-of-hospital management of febrile seizures.

Out-of-hospital providers should try to obtain a brief history of present illness, past medical history (especially for seizures and other neurologic conditions), medications, and allergies while preparing for and during transport. Occasionally, patients initially thought to have febrile seizures turn out to have another disorder, and therefore, evaluating for other causes of seizures, such as trauma or exposure to medications or toxins, is important. A standard out-of-hospital physical examination should be performed with attention toward signs related to a contagious disease (eg, petechial rash), toxidrome, focal neurologic abnormalities, and evidence of trauma whenever possible.

A whole-blood glucose level should be checked in all patients with seizure and persistent altered level of consciousness. Documented hypoglycemia should be treated with intravenous dextrose solutions. Cooling measures and antipyretic administration are not critical interventions for typical febrile seizure and have not been shown to decrease the initial occurrence or recurrence of febrile seizures.^[19]

Out-of-hospital providers should determine whether family members might have already initiated treatment (possibly with rectal diazepam by using the parenteral solution or rectal gel).^{[20] [22]} It is generally agreed that any seizure lasting longer than 5 minutes should be treated, usually with a benzodiazepine as first-line therapy.^[23] Benzodiazepines commonly used in the out-of-hospital setting include diazepam, midazolam, and lorazepam, each with their own cost, storage, and alternative route of administration advantages and disadvantages that are beyond the scope of this review. Several studies

have documented the benefit of benzodiazepine treatment of pediatric seizures in the out-of-hospital setting.^{[24] [25]} Use of a length-based system of medication dosing might be more accurate and faster than age-based or estimated weight-based calculations.^[26] Out-of-hospital providers should anticipate the need for active airway and ventilation support, especially as the seizure persists or additional doses of benzodiazepines are administered. Patients with typical febrile seizures will rarely need more than one dose of a benzodiazepine to terminate the seizure.

In general, all pediatric patients who have had a seizure should be transported by means of advanced life support to a hospital ED, depending on local resources and protocols.

ED evaluation and management

Because the overwhelming majority of febrile seizures will have terminated on presentation to the ED, most patients will not need any stabilization interventions except for minimal airway support during the postictal period. Patients with persistent or recurrent seizures will require more aggressive intervention, and other causes of the seizure should be sought. The treatment of status epilepticus is beyond the scope of this review.

After patient stabilization, the emergency physician should initially focus on signs or symptoms of serious bacterial illness, including meningitis and other potential causes of seizure (eg, trauma or toxic exposure). The history of present illness should include a description of the type of seizure activity, the seizure duration, any postictal neurologic abnormalities, and whether there are any seizure reoccurrences to classify the seizure as a simple febrile seizure or complex febrile seizure.^{[3] [27]} Providers should determine whether the patient has had a prodromal illness and record the duration of the fever leading up to the seizure. Any therapy given at home by the parents-caregivers or out-of-hospital care providers should be documented. The possibility of partially treated meningitis in an infant or child with recent or current antibiotic use should be considered.^{[3] [28]}

Evidence of developmental delay or other underlying neurologic abnormality can be important in giving anticipatory guidance about possible future febrile and afebrile seizures in the patient. A prior history of either febrile or afebrile seizures is also important to elicit the use of chronic medications, especially anticonvulsants. A family history of febrile seizures is helpful because there is a strong genetic component in this disorder.

The role of the physical examination will be to identify a recognizable viral or bacterial illness that might serve as a focus of the fever. The neurologic examination might identify unsuspected evidence of focal deficits (from an intracranial lesion or resultant Todd paralysis from a focal seizure) or increased intracranial pressure (eg, depressed level of consciousness, “sunseting” eyes, papilledema, cranial nerve palsies). Alteration in the patient's general appearance and mental status will signify the immediate need for more aggressive evaluation, such as proceeding with a lumbar puncture and neuroimaging.

Routine laboratory studies are usually not indicated for patients who have had simple febrile seizures, with the exception of a whole-blood or serum glucose test.^{[3] [9] [28] [32]} Patients in this age group with potential electrolyte abnormalities can usually be discerned on the basis of a good history and physical examination and will generally have clinical evidence of significant dehydration, altered level of consciousness, diabetes, or other metabolic disorders.^{[30] [33]}

Further investigation is needed if there is concern about a serious bacterial infection causing the febrile seizure. Patients with simple febrile seizures have similar rates of serious bacterial illness as similarly aged patients who present with a fever and no seizure.^{[9] [10] [32] [33]} Discussion about the evaluation of the well-appearing febrile child is beyond the scope of this article. If meningitis is suspected clinically, then a lumbar puncture is indicated. Patients who present with a simple febrile seizure and a normal history and physical examination result will generally not need any further neurologic workup.

One of the critical decisions that must be made in the evaluation of a child who has had a febrile seizure is whether to perform a lumbar puncture to evaluate for meningitis. Unfortunately, there is little consensus in the literature on this important subject. In 1996, the American Academy of Pediatrics (AAP) issued a practice parameter recommending that a lumbar puncture should be “strongly considered” in patients younger than the age of 12 months with a first febrile seizure and “considered” in those 12 to 18 months of age.^[3] This uncertainty is not surprising because most studies addressing this issue have been retrospective reviews with varying rates of lumbar puncture use and reporting of clinical indicators. There have been no documented cases of occult bacterial meningitis in a patient presenting with a simple febrile seizure, as discussed below. Because many of the signs and symptoms of meningitis in young infants are subtle, most recommendations have been conservative in the absence of large, comprehensive prospective studies addressing this issue.

A retrospective study by Green et al^[28] of 503 patients with a diagnosis of bacterial or aseptic meningitis (115, or 23% of those had a seizure) aged 2 months to 15 years seen in the EDs of 2 referral centers found no cases of meningitis presenting as an isolated seizure. In a second large retrospective study from Saudi Arabia with 200 previously healthy children aged 3 months to 5 years with fever and a seizure, a lumbar puncture was performed in 51% of the patients, yielding 7 (3.5%) cases of meningitis, 3 (1.5%) of which were bacterial.^[34] All of the patients with meningitis had complex febrile seizures, and most had altered sensorium. Another large retrospective study examined the need for lumbar puncture in 452 children aged 6 months to 5 years that presented with fever and a seizure, of whom 15 had meningitis.^[35] A total of 304 (67%) of these patients underwent lumbar puncture, and none that did not undergo lumbar puncture subsequently deteriorated. The authors found that all patients with meningitis appeared “more ill than the physical signs suggested” or had 1 of 3 classic signs of meningitis (ie, photophobia, stiff neck, Kernig sign).

Another retrospective ED-based study of 241 children aged 6 months to 5 years with a first seizure and fever, all of whom underwent lumbar puncture, found that all 11 patients with bacterial meningitis had one of the following factors: (1) a visit to a physician within 48 hours of presentation to the ED; (2) a seizure that occurred in the ED; (3) a focal seizure; or (4) a “suspicious” finding on neurologic or physical examination.^[36]

In summary, a lumbar puncture should be strongly considered in a child younger than 18 months of age having a febrile seizure with (1) a history of irritability, decreased feeding, or lethargy; (2) an abnormal appearance or mental status findings on initial observation of the child (after the postictal period); (3) any physical signs of meningitis, such as a bulging fontanelle, Kernig or Brudzinski signs, photophobia, or severe headache; (4) any complex features; (5) any slow postictal clearing of mentation; or (6) pretreatment with antibiotics. If these factors are absent, then a lumbar puncture can be safely deferred. Children older than 18 months have more reliable signs or symptoms of a CNS infection (altered mental status, meningismus, or both), and a lumbar puncture can be deferred if these are absent. In general, these indications for a lumbar puncture follow what would be recommended for a similarly aged patient with a fever without a seizure. The previously cited literature supports the overall conclusion that patients with simple febrile seizures have the same risk for bacterial illnesses, including meningitis, as similarly aged febrile patients with similar clinical characteristics without a seizure.

The role of neuroimaging before lumbar puncture in the setting of suspected meningitis in children has not been prospectively studied. Several studies have shown little utility in pre-lumbar puncture computed tomography in children, with the exception of patients at risk of cerebral abscess (ie, immunocompromised, focal neurologic findings, evidence of endocarditis) or clinical evidence of increased intracranial pressure (ie, papilledema, obtundation, “sunsetting” ocular motility).^{[37] [42]}

The AAP practice parameter recommends that neuroimaging not be routine for a first-time simple febrile seizure.^[3] An urgent computed tomographic scan of the head without contrast is indicated if the physician is unable to exclude increased intracranial pressure on the basis of physical examination, if the patient has status epilepticus or a complex febrile seizure (especially if there are focal features), if there is evidence of trauma, or if the patient has a cerebrospinal fluid shunt.^[3] Neuroimaging might be indicated for seizure patients with an abnormal electroencephalogram (EEG) result. In some centers, nonurgent magnetic resonance imaging (MRI) might be the neuroimaging modality of choice for evaluation of a seizure in an otherwise stable patient.

Similar to the issue of neuroimaging, the AAP practice parameter recommended that an “EEG not be performed in the evaluation of a neurologically healthy child with a first simple febrile seizure.”^[3] The EEG does not reliably predict which patients with a first febrile seizure will later have epilepsy or even have another febrile seizure.^[3] An EEG might be indicated in patients with evidence of developmental delay, underlying neurologic abnormalities, or a focal seizure. In addition, several studies have called into question the utility of an EEG in children with complex febrile seizures.^{[43] [44]}

Patients who have had a simple febrile seizure usually can be discharged home with appropriate anticipatory guidance about the benign nature of simple febrile seizure, the recurrence risk, and the lack of data supporting aggressive fever control to prevent febrile seizures (Figure). They should have follow-up with their primary care provider for continued evaluation and education. Patients who have had a complex febrile seizure might need admission to monitor for recurrence of seizures, clearing of mental status, and further workup, including MRI, EEG, or both. If discharged, patients with a complex febrile seizure should have follow-up arranged with their primary care provider, a pediatric neurologist, or both for further evaluation.

There are effective prophylactic regimens for febrile seizures to prevent seizure recurrence, but these regimens do not prevent the eventual development of epilepsy, and often, the adverse side effects of the medications outweigh any short-term benefit in preventing febrile seizures.^{[27] [45]} Phenobarbital is effective in preventing febrile seizures but has serious adverse effects, such as hyperactivity, hypersensitivity reactions, and possible loss of cognitive function. Valproic acid is similarly effective in preventing febrile seizures but is associated with hepatotoxicity, thrombocytopenia, weight changes, gastrointestinal disturbances, and pancreatitis and involves close monitoring with frequent blood sampling.^{[17] [46] [48]} Oral diazepam at the first sign of a febrile illness has been effective in preventing febrile seizures in some but not all studies and has predictable sedative adverse effects.^{[49] [51]} Antipyretics are not effective in preventing febrile seizures.^{[19] [50] [52]} There is a strong consensus in the literature not to offer prophylactic medications for simple febrile seizures, leaving the issue of complex febrile seizures up to the practitioner.^{[27] [45]}

In summary, febrile seizures are a common pediatric presentation in both the out-of-hospital and ED settings. Most patients who fit the diagnosis of a simple febrile seizure will need little more than a good history and physical examination, blood glucose documentation, minimal supportive care, treatment of any infectious causes, and reassurance and anticipatory guidance to the child's caregivers. A low threshold to perform a lumbar puncture in younger infants, patients receiving antibiotics, and patients with a slow return to normal mental status needs to be maintained. Patients with a complex febrile seizure usually require neurodiagnostic workups, including a neuroimaging study, a lumbar puncture, and EEG, and should be referred to the primary care provider or appropriate subspecialist for ongoing care. Febrile seizures generally have a benign prognosis and prophylaxis, with anticonvulsants and antipyretics not indicated.

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