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Evidence-based Management of Children with Febrile Seizures

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Febrile seizures (FS) are the most common form of childhood seizures.[1] Globally, they affect as few as 1.5% of children in China and as many as 15% of children in India, Japan, and Guam.[2] They have been estimated to be present in 2-5% of children younger than age 5 in the United States and Western Europe.[3]

The peak incidence of FS occurs at approximately 18 months of age, with most seizures occurring between the ages of 6 months and 5 years. They are more common in boys than in girls. Febrile seizures occurring in patients younger than 3 months and older than 7 years of age are uncommon. The rate of febrile seizures is highest in the winter, with a seasonal peak in January and a daily peak in the evening from 6 p.m. to midnight, correlating with a circadian variation in temperature amplitude.[4] The authors review an evidence-based approach to the child with a febrile seizure.

— The Editor

Approach to the Child with a Febrile Seizure

Febrile seizures are a particularly alarming event for a caregiver to witness. They also can pose a diagnostic conundrum for the emergency physician, whose job it is to stabilize the actively seizing child, diagnose him or her, and treat any underlying conditions. The bedside evaluation and management of the seizing febrile child involves certain responsibilities for the physician. This article sequentially follows and expands upon these responsibilities, which are outlined in Table 1.

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Provide Supportive Care

The approach should be no different than that practiced with any other sick child. If the patient is actively seizing, the clinician should maximize control of the airway using techniques such as chin lift or jaw thrust or lateral decubitus positioning or using airway adjuncts such as a nasopharyngeal airway. Oxygen should be provided by facemask if the patient's oxygen saturation drops below 92% on room air. Intravenous (IV) access should be gained at the earliest opportunity for the administration of medications and to obtain any needed blood work. A benzodiazepine should be administered for an acute seizure; further antiepileptic medication should be considered if the seizure activity persists (see section titled *"Determine the need for medications")*.

Similar principles hold true for the child who presents in a post-ictal state. If the child is maintaining his/her airway with normal oxygen saturation, observe the patient and take appropriate precautions. Be sure there is someone to monitor the child and observe for further seizure activity.

Allay Caregiver Anxiety

Once the child has been stabilized, attention next should be directed to the caregiver who was with the child at the time of the event. The adult who witnesses a seizure is uniformly disturbed by the event, and almost one-third of caregivers who witness their child's seizure report fear that their child was dying during the event.[5,6] This fear persists beyond the cessation of motor activity and lessens only with the patient's progressive return to a normal mental status. Witnessing a febrile seizure can result in the development of physical or psychological ailments.[7]

At the time of the emergency physician and caregiver interface, the caregiver may appear distraught or calm. In both circumstances, it is best to ask the caregiver, "What were you thinking when you saw the seizure?" This may permit them to express their fears and concerns.

Extract History

Once the caregivers have expressed their fears and concerns, obtaining accurate information surrounding the event from them is crucial. The information gathered on initial presentation will guide further interventions in the ED. There are three periods of time that should be differentiated during the discussion with the caregivers, including: the pre-seizure, the seizure itself, and the post-seizure. All of the periods may serve to guide the physician's concern for the presence of an underlying serious infection as a cause of the event.

History of Present Illness. First, in the pre-seizure time period, determine if the child was previously well, when the caregivers first noticed signs of an illness, and whether the child had any physician visits in the preceding days due to an illness. Not uncommonly, a FS will be the first manifestation of an illness, and it can occur before the caregiver even knows the child has an elevated temperature.

Determine if the child has recently finished or is currently receiving any treatments, such as antibiotics or antipyretics, or has recently received any vaccines. Ask the caregiver if they have been recording temperatures at home and what method was used (oral, axillary, rectal), also include questions about the fever height and duration. Gather information about any signs and symptoms of serious illness, such as lethargy, decreased urine output, or petechial rash. Exposure to a potential contagion within the family or outside of the family can be a clue to the etiology. Any recent trauma, daycare attendance, and any exposure to adult prescription medications or other toxic ingestions all are important parts of the patient history.

Next, clinicians should formulate the information surrounding the actual event. Find out what attracted the caregiver's attention to the child, and the location where they found the child. Any description of a noise or commotion that causes the caregiver to investigate should raise suspicion for a fall or trauma, especially if the child is found near stairs. While it may be difficult for the caregiver to recall, ask them what they observed at the time of the event. In the course of a febrile seizure, there may be any combination of frightening events that the caregiver witnesses and may describe. These may include primitive grunting, eye deviation, blank stare, inability to fix and follow with the eyes, drooling, apnea, cyanosis, stiffening, shaking, involuntary release of stool and urine, or unresponsiveness. Ask the family to describe the seizure activity. Was the child's entire body shaking or a single body part (e.g., arm)? Was the child responsive or unresponsive?

Finally, inquire about post-ictal activity. Ask how long the seizure lasted, what happened after the child stopped shaking,

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Table 1. Emergency Physician Responsibilities for the Febrile Seizure Patient

- ❑ Provide supportive care
- ❑ Allay caregiver anxiety
- ❑ Extract patient history
- ❑ Perform physical examination
- ❑ Categorize the seizure
- ❑ Consider precipitating causes
- ❑ Determine the likelihood of an intracranial infection
- ❑ Determine likelihood of an extracranial, serious bacterial infection (SBI)
- ❑ Establish a differential diagnosis
- ❑ Determine the need for medications
- ❑ Determine if diagnostic studies are warranted
- ❑ Share the natural history with the caregiver
- ❑ Know prophylactic options
- ❑ Determine the disposition
- ❑ Provide specific discharge instructions
- ❑ Complete the medical record

and about the patient's mental status in the immediate and delayed post-event period.

Prehospital providers can be a valuable source of information for all three time periods (pre-seizure, seizure, and post-seizure). They often get first-hand accounts by witnesses at the scene about how the child was acting prior to and during the seizure. Their contact and run times may help construct a time frame of events and the actual duration of the seizure activity. They may additionally shed light on the mental status of the child upon their arrival at the scene and to the ED. Before they leave the ED, seek out their perceptions about the event and information surrounding the condition of the home, such as open bottles or containers and the demeanor of the caregivers at the scene.

Past Medical History. Clinicians should gather information from the caregivers about a prior history of febrile or afebrile seizures, as well as history of developmental delay or other underlying neurologic abnormalities. Determine the use of medications, specifically focusing on the past or current use of anticonvulsants and any recent antipyretic doses. Review the birth history, including maternal and neonatal factors. Factors associated with the occurrence of a first-time febrile seizure include a prolonged hospitalization after birth, developmental delays,[8,9] and premature delivery.[10] *(See Table 2.)* Other risk factors include maternal smoking,[11] day care attendance,[8] and maternal hormonal therapy for infertility.[12] Obtain a surgical history, including any neurosurgical procedures, as this may increase the risk of non-febrile seizure.

Family History. Genetic contribution is a proven, yet poorly understood mechanism for the development of FS. Numerous chromosome linkages have been implicated, but no single mutation can predict who will develop a FS. Still, one of the most identifiable risk factors is a family history of FS,[3] with the highest risk occurring in children who have a first-degree relative with a history of FS.[8,9,13] The risk of FS in siblings is between 10% and 45%,[14] but is higher in monozygotic twins and is doubled when both parents have a history of FS.[3]

Perform Physical Examination

The physical examination of the child with a FS begins with evaluation of their general appearance, vital signs, and mental status. The child brought to the ED for FS often will present after the event has occurred and will likely be in a post-ictal state.[15] This state should resolve after a short period of time.

Determine if the child appears toxic or nontoxic. Clues to a toxic child include signs of poor perfusion, altered motor tone, abnormal cry, lethargy, and abnormal respiratory rate or pulse. Acute bacterial meningitis (ABM) must be considered in a patient who presents with a fever that is accompanied by a seizure. High-risk historical and examination features of ABM are listed in *Table 3*.

Initial core temperature should be recorded, preferably a rectal temperature reading. It should be recognized that temperatures taken by caregivers or by pre-hospital personnel can be misleading if taken before the peak of the fever. Perform a physical exam, focusing on common sources of fevers in children, such as acute otitis media or upper respiratory tract infections. If a source of infection is found, the clinician should determine if the child is sicker than what would be anticipated from that focus of infection. Physical exam signs that should prompt further evaluation and a search for a more serious source of infection include: toxicity; prolonged post-ictal lethargy; focal neurologic deficits; Todd paralysis; or signs of increased intracranial pressure, such as papilledema, altered mental status, or cranial nerve abnormalities.[15]

Categorize the Seizure

There are two definitions of FS established in the literature. The first definition was part of a National Institutes of Health (NIH) consensus statement on febrile seizures.[16] Their definition was "an event in infancy or childhood, usually occurring between three months and five years of age, associated with fever but without evidence of intracranial infection or defined cause." It excluded children with previous nonfebrile seizures. A more recent definition was set forth by the International League Against Epilepsy. Their definition was a seizure "occurring in childhood after age 1 month, associated with a febrile illness not caused by an infection of the central nervous system, without previous neonatal seizures or a previous unprovoked seizure, and not meeting criteria for other acute symptomatic seizures."[17] An important determination to make in the child who seizes is whether they are febrile. Both of the definitions noted previously acknowledge that a fever has to be a part of the illness, but neither indicate a specific cut-off for the height of the temperature. In general, fever has been defined as a rectal temperature $\geq 38^{\circ}$ C.[18] The patient with a temperature $\leq 38^{\circ}$ C who has seized has not likely experienced a febrile seizure.

Febrile seizures can be classified as simple or complex. Simple febrile seizures are the most common, and comprise 75% of febrile seizures.[19] A simple febrile seizure is generalized, brief, and

Table 2. Risk Factors for Febrile Seizures

FIRST FS	RECURRENT FS	EPILEPSY RISK
Family history, 1st degree	Family history, 1st degree	Family history of epilepsy
Developmental delay	Onset < 18 months	Neurologic abnormality
Maternal smoking	Lower temperature around 38° C	Short fever duration before seizure
Daycare attendance	Short fever duration (<1 hour) before seizure	Complex seizures
Infertility treatment		
Prematurity		

Adapted from references: 1, 92

does not recur within 24 hours.[9,17] Most definitions of simple FS describe the event as lasting less than 15 minutes, but this number is ill-defined. Approximately 87% of children have a seizure duration of less than 10 minutes, but caregivers, in an anxious state, often exaggerate the estimated length.[19] Complex febrile seizures are prolonged (defined as > 15-20 minutes), with focal signs and/or recurrence within 24 hours or within the same febrile illness.[3,17] From a practical standpoint, if the prehospital providers find the child actively seizing, or if the transported patient is seizing upon arrival to the ED, consider this a complex FS.

Consider Precipitating Causes

There is no clearly identified mechanism by which a febrile illness causes convulsions. Gene mutations found in patients with febrile seizures have provided support for the role of genetics in those with a family history of febrile seizures, although the mechanism has not been identified.[20] While genetics may eventually explain familial cases, other investigators have postulated a number of theories for febrile seizures, including a rapid rise in temperature,[21] respiratory alkalosis,[22] and direct viral mediated affects on the brain.[23] No single mechanism has been proven in multiple studies, indicating a likely polymorphic etiology of febrile seizures.

Immunizations. Fevers are a common sequela of childhood immunizations and have, therefore, been implicated as a cause of febrile seizures. It is unclear, however, whether it is the vaccine components or the fever induced by the vaccine that precipitate the seizure. Vaccines that have been implicated include the measles, mumps, rubella (MMR);[24,25] diphtheria and tetanus toxoid, pertussis vaccine (DTP);[26] and pneumococcal 7-valent conjugate vaccine.[27]

Viral Illnesses. Systemic viral illnesses commonly are associated with febrile seizures.[23] Some of the more recognizable viruses isolated from febrile seizure patients include influenza A,[28,29] cytomegalovirus, respiratory syncytial virus,[23] human herpes virus-6 (HHV-6), and HHV-7.[30-32] Epstein-Barr virus has been associated with encephalopathic infections in pediatric cases,[33] and rotavirus has been found in the cerebrospinal fluid (CSF) of patients with febrile seizures.[34] In one institution, the most common pathogens isolated in 923 children admitted with febrile seizures included: influenza (17.6%), adenovirus (6.8%), parainfluenza (6%), respiratory syncytial virus (RSV) (2.7%), and rotavirus (1.3%).[35] Due to numerous variables, it is difficult to determine the true incidence of viral pathogens as the cause of febrile seizures.

Bacterial Illnesses. Bacterial etiologies of FS are less common than viral infections. *Shigella* species, a well known cause of FS, has been reported to cause seizures in up to 12-45% of affected children.[36] In one study, 23% of patients with culture-proven *Shigella* suffered at least one seizure.[37] These patients are classically recognized by the presence of dysentery, fever, and seizures, although seizures can predate the diarrheal part of the illness. Their course frequently is benign.[36] *Streptococcus pneumoniae* is another pathogen that is known to be associated with febrile seizures.[38]

Determine Likelihood of Intracranial Infection

After a history has been taken, a physical examination completed, and consideration given to the potential etiologies of the event, the physician should then provisionally determine whether the febrile patient truly had an apparent FS. The term "apparent" is used as the patient, by definition, must be free from infection of the central nervous system (CNS).[16,17] In most cases in which a FS does occur, the history and physical examination are sufficient to clinically exclude a CNS infection.[39] The most notable CNS infection to be excluded is ABM. The incidence of ABM prior to the conjugate *Haemophilus influenzae* and the pneumococcal 7-valent conjugate vaccines was between 2% and 5% in children with a complex FS.[1] Since the introduction of these vaccines, the incidence has been reported at 0.4-1.2%, although certain clinical features can increase the risk for ABM.[40-43] The features that increase the risk for ABM in patients with an apparent FS can be identified via the general history, the seizure pattern, and certain physical examination features. *(See Table 3.)* In circumstances of uncertainty, lumbar puncture and analysis of cerebrospinal fluid will be required.[44]

Determine Likelihood of an Extracranial SBI

After intracranial infection is considered, focus on determining the likelihood of extracranial serious bacterial infections (SBI). Extracranial SBIs include occult bacteremia (OB), pneumonia, osteomyelitis, pyarthrosis, pyelonephritis, and enteric pathogens. The risk of extracranial SBI in the child with a first-time FS is no different than for the non-seizing febrile patient.[45] Seizures may be found with an OB from *Streptococcus pneumoniae*,[38,45] *Shigella* species,[36,37] and *Neisseria meningitidis.* Seizures can be associated with non-bacteremic shigellosis.[36,37]

Establish a Differential Diagnosis

The differential diagnosis of FS should include any condition that presents as fever plus a potential seizure. The illnesses that masquerade as febrile seizure can be divided into those illnesses that simulate either simple or complex febrile seizures, or they can have features that overlap. *(See Table 4.)* The various febrile

Table 3. Features that Increase the Risk for Acute Bacterial Meningitis in Patients with Apparent Febrile Seizure

GENERAL HISTORY	SEIZURE PATTERN	PHYSICAL EXAMINATION
Age ≤ 12 months	Focal seizure	Blunted response to overture
Exposure to invasive disease	Motor, speech, or vision deficit	Poor perfusion
Ill at least 3 days	Multiple seizures	Generalized petechiae
Physician visit in antecedent 48 hours	Prolonged seizure	Altered motor tone
Documented bacteremia	Field or ED anticonvulsants	Abnormal cry
On antibiotics for extracranial infection	Prolonged post-ictal phase	Hard to console
Immunocompromised		Inability to fix and follow with eyes
Neurosurgical procedures, hardware		Nuchal rigidity
Penetrating head trauma		Full fontanel
		Focal neurologic deficit

diseases that resemble FS rarely have seizures as the sole manifestation of the presenting complaint.[39,46]

Determine the Need for Medications

Emergency physicians and prehospital personnel typically will encounter a post-ictal child who presents after a single, first-time febrile seizure.[15] These seizures typically last < 10 minutes and resolve spontaneously before arrival to the ED.[3] If the child is not seizing upon the arrival of prehospital personnel at the scene and remains seizure-free during transport, the child requires no prehospital medications to prevent further seizure activity.[15] In the ED, if the child is gradually regaining consciousness and has no reported seizure recurrence, they require no further therapy.

For children who have witnessed, continuous seizure activity of more than 10 minutes duration, numerous options exist to terminate the seizure activity. *(See Table 5.)* If an IV is established, the most common first-line agent is lorazepam, which also can be administered by the intramuscular (IM) route.[47] An alternative medication is diazepam, which can be given intravenously, but is regularly used by caregivers out-of-hospital via the rectal route as a first-line medication.[48] Midazolam has been shown to be at least as effective as diazepam in the management of seizures, and it can be administered via IV, intranasal (IN), or buccal routes.[49-53] Both IN and buccal administration use the IV formulation. The IV liquid is sprayed into the nose as a mist using an atomizer or can be inserted into the mouth between the buccal mucosa and the teeth.

There is a subset of children (about one-third) who have recurrent FS during the same illness.[54] When these children regain normal neurologic function between events and present awake and without seizure activity, no further treatment is required at that time. Consideration should be given to the use of anticonvulsants to prevent future recurrences, but this should be done in consultation with their pediatrician or specialist (see section titled *"Know prophylactic options"*).

Children who do not regain normal levels of neurologic function between seizures, or who have seizure activity that persists longer than 30 minutes, by definition are considered to have status epilepticus (SE).[17] These patients need aggressive treatment to stop the seizure activity. Febrile SE should be treated in the same manner as non-febrile SE, up to and including general anesthesia and definitive airway management.[47] Discussion on the management of SE is reviewed elsewhere and is beyond the scope of this article.[55,56]

Antipyretics should routinely be given in the form of acetaminophen or ibuprofen orally to the febrile child who is awake, or by administering acetaminophen rectally if the child remains post-ictal. This will improve the child's comfort and provide comfort to the caregiver. A common assumption held by caregivers and medical personnel is that the use of antipyretic medication to lower the temperature will prevent seizure recurrence. Factually, the reduction of the temperature with antipyretic medications has never been shown to reduce subsequent febrile seizures.[57,58]

Determine if Diagnostic Studies are Warranted

Diagnostic tests may be of utility in the search for the source of fever in a young child without an apparent focus of infection. It is believed that this holds true for those febrile children who seize. Unfortunately, the usefulness of specific diagnostic studies in the febrile subset of children who seize has not been vigorously examined. In the 1970s and 1980s, this led to variable, but frequent use of diagnostic tests and a plethora of conflicting recommendations.[59] Practice variation has been documented into this millennium.[60] Some of the variations can be explained by persistent uncertainty regarding the utility of a specific test. Other variabilities result from misunderstanding the magnitude of risks associated with a febrile seizure. The following historical and current analyses are offered to clarify existing diagnostic dilemmas.

Complete Blood Count (CBC). *History*. In the 1970s, the CBC was held as a strategic laboratory investigation for the evaluation of the febrile pediatric patient without focus of infection. In that decade, authors had suggested a CBC held utility for patients with febrile illness who seized. In the late 1980s and early 1990s, authors questioned the value of a CBC in acute febrile seizures.[61,62]

Reasoning. The evidence-based utility of a CBC with acute febrile seizure should be based upon data from comparable patients without seizure and from febrile seizure patients.

1. Febrile without seizure. It has long been held that CBCs are useful to evaluate the cause of fever in febrile children. The premise may be a result of suggestions that bacterial diseases, but not

Table 4. Differential Diagnosis of Febrile Seizures

MASQUERADING AS SIMPLE	MASQUERADING AS COMPLEX	OVERLAPPING FEATURES
Viral meningitis	Hemiplegic migraine	Occult closed head injury
Shigellosis	Moya moya disease	Acute demyelinating disease
Salicylism	Brain abscess	Periarteritis nodosa
Lead intoxication	Viral encephalitis	Systemic lupus
Neuroleptic malignant syndrome	Acute bacterial meningitis (ABM)	CNS tumor with bleed
Antidepressant overdose		

viral, cause an elevation of total white blood cell count, elevation of neutrophilic count, and a shift toward immature cells. Unfortunately, this is untrue. Based on the analysis of the CBC, one cannot discriminate a disease process of bacterial origin from that of viral origin.[63] The degree of neutrophilia (≥ 10,000-10,500), and to a lesser extent the total elevation of the white blood cell count (> 12,500-15,000), are predictive of an increased *likelihood* of OB in the clinical setting of acute febrile illness without focus in a well-appearing child between ages 3 and 36 months with temperatures ≥ 39.2-39.4° C.[64] This association is greatest for those infants between ages 6 and 24 months who are febrile, with temperatures ≥ 40° C.[65] However, in the pneumococcal conjugate vaccine era, these markers may not have as high a predictive value.[66,67]

2. Febrile seizure. In adult humans, long lasting convulsions without fever are associated with peripheral leukocytosis. In children, febrile seizures have a limited impact on the total peripheral blood count. Approximately 60% of patients have normal blood counts. Of those with mild to moderate leukocytosis, neither the temperature elevation nor the type of seizure or duration of seizure is associated with specific elevations of the white blood cell count.[68] The total leukocyte count in patients with febrile convulsions from shigellosis is usually within normal limits, but the differential count characteristically shows a marked shift to increased band forms.[36] Other data on the differential count with acute febrile seizures is lacking.

In studies of occult bacteremia (OB) with FS, conflicting data on leukocyte changes has been found. Some investigators in pre-pneumococcal 7-valent conjugate vaccine usage have seen an association of leukocytosis and bacteremia. As an example, Chamberlain and coworkers found the mean leukocyte count was 20,900 mm^3 in those with OB compared to 13,100 in those without OB.[69] Other studies have shown no association of leukocytosis and bacteremia in patients with FS. As an example, Shah found there was no difference in white blood cell count between patients who were later identified to have bacteremia and those with negative cultures.[38]

Our Recommendation. Clinicians who expectantly treat well-appearing, febrile pediatric patients without apparent focus of infection should base their decision on whether to plate a blood culture and administer parenteral antibiotics on the results of the screening CBC. Patients they treat who seize should be managed in the same fashion. Clinicians who routinely do not utilize the CBC as a screening tool for submission of a blood culture should not acquire a CBC in the patient who seizes.[70]

Blood Chemistries. *History.* In the mid-1970s, many physicians routinely ordered a full battery of serum chemistry tests for the child with FS. In the last decade, the trend has been to restrict blood chemistry testing. The transition has been a result of evidence-based literature leading the American Academy of Pediatrics to recommend that serum chemistries should no longer be part of a routine evaluation for the child with a first, simple febrile seizure.[71]

Reasoning. In population-based studies of children with simple febrile seizures, abnormalities are not found in serum phosphorous, magnesium, or urea nitrogen.[72] Asymptomatic, insignificant reduced calcium levels are infrequent.[73] Euglycemia is relatively constant, although stress-induced asymptomatic hyperglycemia occasionally may occur.[73] Hyponatremia, hypokalemia, or hypoglycemia are infrequent and are found in circumstances of abnormal fluid consumption, fluid loss, or poor nutritional intake in the prodromal phase of an acute febrile illness. These abnormalities can be anticipated on clinical grounds, independent of the occurrence of the seizure.

Our Recommendation. As a general rule, blood chemistries should not be obtained. On the basis of history and physical examination, in light of specific clinical scenarios, selected blood chemistries are warranted. Obtain electrolytes, BUN, creatinine, and a bedside glucose oxidase test in individuals who have evidence of moderate to severe dehydration. Obtain a bedside glucose oxidase test in the face of altered mental status.

Blood Culture. *History.* In pre-*Haemophilus influenzae* b (Hib) vaccination era, occult bacteremia (OB) was present in 2.7-7% of patients with febrile seizures.[69,74,75] Following the introduction of the Hib vaccination, rates of OB in febrile children without seizures decreased. Similarly, rates of OB in patients with febrile seizures declined. In the post-Hib/pre-pneumococcal vaccination era, the rates of OB ranged from 2.1% to 2.9%.[38,76] The majority of cases were caused by *Streptococcus pneumoniae* of the serotypes included in the heptavalent pneumococcal conjugate vaccine.[77] In the post-pneumococcal 7-valent conjugate vaccine era, bacteremia has become a rare event in previously-healthy, young children evaluated in the outpatient setting. For those between age 3 and 36 months, with and without an apparent focus of infection, OB has been eradicated in one study.[78] The maximal rate of OB in a study was 0.7%.[79] OB has been caused by *S. aureus, N. meningitidis,* and non-vaccine serotypes of *S. pneumoniae*.[67]

Reasoning. A physician cannot accurately predict which well-appearing febrile pediatric patient without apparent focus of infection will have OB. The highly febrile patient who has received at least one pneumococcal 7-valent conjugate vaccine dose has a < 1% risk of OB, and the organism recovered is unlikely to be an invasive strain of *Streptococcus pneumoniae.* The patient who has

Table 5. First-line Benzodiazepines for the Management of Febrile Seizures

MEDICATION	DOSE	ROUTE
Lorazepam	0.1 mg/kg	IV/IM
Diazepam	0.3 mg/kg	IV/IM
	0.5 mg/kg	Rectal
Midazolam	0.1 mg/kg	IV
	0.15 mg/kg	IM
	0.2 mg/kg	Intranasal
	0.3 mg/kg	Buccal

Adapted from references 49, 50, 52, 53, 55, and 56

received pneumococcal 7-valent conjugate vaccine and has seized has the same risk of pneumococcemia as the comparable febrile patient without seizure.[80] If the physician feels a blood culture has clinical utility in the outpatient management of a febrile pediatric patient, the occurrence of the seizure should not alter the decision to acquire a culture. If the physician feels outpatient blood culturing is not of cost benefit for febrile children, the physician should not acquire a blood culture in a febrile pediatric patient who seizes.

Our Recommendation. Blood culturing in the face of a febrile seizure should be performed only if the clinician routinely performs a blood culture in the course of the evaluation of a comparable febrile child without seizure.

Urinalysis and Culture. *Background.* Urinary tract infection (UTI) is a well-recognized, focal, serious bacterial infection in the well-appearing febrile child without an apparent focus of infection. The overall incidence of abnormal urinalysis and positive urine cultures ranges from 3% to 6% in highly febrile males and females younger than age 2.[81] A similar incidence of UTI would be predicted for matched controls who have seized. One study did confirm a lower rate of UTI of 0-7%.[76]

Our Recommendation. Clinicians should obtain a catheterized urine specimen from females with temperatures ≥ 40° C (hyperpyrexia) and in male infants younger than age 6 months who are circumcised, as well as in males younger than age 12 months who are uncircumcised. A catheterized urine specimen also should be obtained from all pyrexic females younger than age 1.

Lumbar Puncture. *History.* Unless contraindicated, lumbar puncture (LP) has been advocated for all febrile patients who have clinical characteristics that increase their likelihood for acute bacterial meningitis (ABM). *(See Table 3.)* Seizures are seen in 12-20% of patients with ABM.[82] The majority of seizures with ABM occur within the first 24 hours of diagnosis; they often are the clinical attribute that precipitates the ED visit. The historical onus has been on the emergency physician to exclude ABM when presented with a febrile child who seizes.

One of the conventions in the 1970s to1980s was to perform a LP on all first-time febrile seizure patients, irrespective of age. Those who advocated its performance only at the first seizure erroneously implied that those with recurrent seizures with fever were at no risk for ABM who, therefore, did not require a LP. We know now that the clinician must maintain as high an index of suspicion for ABM in a patient with a past medical history of febrile seizures as he or she would with the first episode.

The second convention from the 1970s that has taken three decades to change is an automatic age below which to perform a LP. Eighteen months of age for a first febrile seizure became embedded in the literature as the result of a single retrospective study by Samson and colleagues in 1969.[83] In their study, the authors found 11 infants (average age, 8.2 months) with ABM who had seized. They lacked nuchal rigidity, Brudzinski's sign, bulging fontanel, or depressed sensorium. All without clinical evidence of meningitis were younger than 16 months of age. The authors arbitrarily set an age of 18 months as the recommended age for LP for infants with a constellation of seizure and fever.[83] In the decade that followed, Gerber and Berliner reported on 81 infants who were free of clinical evidence of meningitis with a first febrile seizure. All of their LPs were negative.[84] Despite additional studies over successive decades with similar negative results, an age cutoff of 18 months has persisted in some recommended sources.

The third convention, to consider a LP on the basis of clinical features associated with the seizure, has had a more rapid evolution. Currently, it is more common to let the history of present illness and physical examination findings serve as determinants for the performance of the LP.

Reasoning. The experienced physician no longer blindly performs a LP if the patient presents with a clinical picture that is incompatible with ABM. In support of this concept, Rutter and Smales, on the basis of clinical information, were able to select infants who were at high risk of ABM.[85] Lorber and Sunderland reported that an experienced clinician, on the basis of history and physical examination, could successfully identify all cases of ABM.[86] Rosenberg and coworkers found that in the absence of prior antibiotic therapy, an experienced clinician could clinically detect which patients were at high risk of ABM.[87] Jaffe and researchers retrospectively determined that five historical and physical examination items discriminated between children with and without meningitis. These included a physician visit within 48 hours, the occurrence of seizure upon arrival to the ED, a focal seizure, or abnormal findings on general physical or neurologic examination. Findings of rash (including petechiae), cyanosis, hypotension, and grunting respirations, used in combination with an abnormal neurologic examination, identified all children with ABM and spared 62% of children without ABM who received LP.[88]

Various authors have reexamined the age at which a LP should automatically be done. On one end of the spectrum, some support the clinician's ability to identify those febrile patients with seizure secondary to ABM in children > 6 months of age.[86,89] On the other hand, The American Academy of Pediatrics in their Practice Parameter recommended an LP be considered in children between age 12 and 18 months and performed automatically in infants younger than age 12 months.[71]

Our Recommendation. LP should not be routine for children with febrile seizures. LP should be reserved for those patients who have characteristics that increase their risk for ABM. These historic

features include the recent environment (infectious exposures, recent illness, physician interaction, use of antibiotics) and evolution of the illness, including the attributes of the seizure itself. Other features include physical examination findings. *(See Table 3.)*

Chest Radiography. *Background.* Chest x-rays typically will confirm pneumonia in a febrile child with fever, cough, tachypnea, and auscultatory findings. Chest films will uncover an occult pneumonia in 1-3% of well-appearing, young febrile children without an apparent focus of infection.[81] It has been suggested that pneumonia, like other serious bacterial infections, occurs with rates similar to those seen in matched cohorts who present with fever and no seizure.[61,62,69] A finding of 6% of patients with pneumonia who had acute febrile seizures is consistent with this premise.[45]

Our Recommendation. Clinicians should acquire a chest x-ray in the same fashion for the evaluation of a febrile child who seizes as they would in their assessment of the acute febrile child without focus of infection who has not seized.

Neuroimaging. *Background.* Neuroimaging with simple febrile seizure will not uncover a clinically important intracranial pathology. Mass lesion, hemorrhage, hydrocephalus, or cerebral edema are not likely to be found in children who sustain a simple febrile seizure or a complex febrile seizure and who are neurologically normal on exam.[90,91]

Our Recommendation. Space-occupying intracranial pathology will not be uncovered in a child with a simple or complex febrile seizure. Neuroimaging is, therefore, not warranted, except in a child with congenital heart disease who is at risk for brain abscess.

Share the Natural History with the Caregiver

Caregivers should not be told that a seizure will never recur. They should be informed that a seizure can occur again, either in the course of the current illness or in future febrile illnesses. One-third of children will experience at least one recurrent FS.[54,92] Up to 50% will occur in the first year after their initial FS, and more than 90% in the first two years. The strongest risk factors for recurrence appear to be the age at which the first seizure occurs, commonly < age 18 months, and a family history of FS.[1,92] Other predictors place children at higher risk for the development of future seizure. *(See Table 2.)*

For children without a history of afebrile seizures, a simple FS increases the risk of afebrile seizures (epilepsy) later in life.[93] A recent study found that after 23 years of follow up, the risk of developing epilepsy was 6.9% in children with febrile seizures, compared to 1.8% for children in the general population.[94] Children with a family history of epilepsy, cerebral palsy, or low Apgar scores at 5 minutes were at increased risk. Another study found that risk factors included neurologic abnormality, family history of epilepsy, and short duration of fever (< 1 hour) before seizure development. Two of these risk factors resulted in a 17-22% risk of epilepsy and the presence of all three increased the risk to 49%.[93]

Know Prophylactic Options

The prophylactic treatment to prevent recurrent febrile seizures is a controversial subject matter, and recommendations for the routine use of antiepileptic medications are not clear. A historical and current review of the literature is included in this section.

Background. The use of anticonvulsants as prophylaxis after a febrile seizure has changed dramatically over the last 30 years. Prior to the 1970s, children were routinely treated after only a single episode. This gradually changed over time to treatment of children only after a recurrent FS and then, in the 1990s, prophylaxis became a rarity.

Reasoning. Current consensus is that in view of the benign nature and low risk of complications in most simple febrile seizures, there is probably not a need for long-term medication in the overwhelming majority of individuals. It is acceptable for an emergency physician to defer the decision to start prophylactic medications to the child's primary care physician (PCP). There is, however, no reason emergency physicians treating the child should not be aware of treatment options, and even choose to start prophylaxis under the appropriate circumstances. Careful decision-making about starting these medications should involve the caregivers and the child's PCP or specialist because of the potential side effects.[95] Caregivers should be informed that while these medications can reduce the recurrence of FS, they have no effect on the potential development of epilepsy later in life.[96-99]

Treatment Options. Prophylactic treatment options can be used in two different ways, depending on the medication. The first option is dosing intermittently at the onset of a febrile illness. The second option is daily dosing. Both have been shown efficacious in preventing FS, and the medications used in both circumstances will be discussed.

Continuous Phenobarbital. Daily phenobarbital has been shown to be effective for reducing the risk of recurrent febrile seizures.[57,100-102] Sedation is common for the first 2-3 weeks and transient or prolonged, but reversible, behavioral aberrations occur in 25-40%. Phenobarbital is not effective for reducing the risk of recurrent febrile seizures when dosed intermittently at the onset of a febrile illness.[103]

Continuous Valproic Acid. In randomized, controlled studies, valproate has been shown to be effective in the prevention of recurrent febrile seizures compared to phenobarbital and placebo.[104,105] The dose is 20-40 mg/kg per day, given as divided doses. Therapy with valproic acid has been associated with fatal hepatotoxicity, thrombocytopenia, weight loss and gain, gastrointestinal disturbances, and pancreatitis. These side effects have limited its use as continuous therapy.

Intermittent Benzodiazepines. Diazepam can be given rectally (5 milligram suppositories) or orally (2 or 5 milligram tablets) at the onset of a febrile illness.[106,107] One large, randomized, placebo-controlled trial demonstrated that oral diazepam, when given at the onset of febrile illness, showed a reduction in the rate of recurrent febrile seizures at follow up.[95] Limitations to intermittent use include failure to recognize a fever by the caregivers prior to the seizure. Benefits include reducing cost

and potential drug toxicity and obviating the need for daily medication administration.

Other antiepileptic medications, such as phenytoin and carbamazepine, are ineffective for preventing recurrence of febrile seizures.[1]

Our Recommendation. Febrile seizures are a common, benign event in children, and most children do well. There are medications available that will reduce the incidence of recurrent FS, but the benefits must be weighed against the potential adverse effects of the medications. We recommend against the use of antiepileptic therapy in a child with a simple FS. Emergency physicians should defer the prescribing of prophylactic medications to the child's PCP, yet be knowledgeable about the use and purpose of using these medications.[108] Similar recommendations have been made by the American Academy of Pediatrics.[109,110]

Determine Disposition

The emergency physician must consider multiple factors to make an appropriate disposition judgment for the child who seizes in association with a febrile illness. After addressing medical issues and social concerns, the emergency physician can safely discharge a majority of patients with febrile seizures. Admission to an observation unit or short-stay (less than 24 hours) unit may be an acceptable alternative in the following circumstances.

- **Physician preference.** There is a practice variation in the management of febrile seizure patients. Primary care physicians differ[70] as do emergency physicians[60] in their approaches to a home-going disposition. The emergency physician should respect the disposition strategy of another physician who wishes admission.
- **Clinical state.** Any attribute that increases the physician's uncertainty for the possibility of serious infectious disease is an indication for continued observation of the patient. These circumstances include young age (≤ 6 months), prolonged postictal phase, complex seizure, and underlying diseases.
- **Caregiver concerns.** Continued observation may be necessary if the patient's caretaker is unable to cope or provide appropriate observation of the child. Hospitalization also may be necessary if there are questionable parenting skills, lack of transportation, or a prolonged distance to medical care.

Provide Specific Discharge Instructions

Amplify at discharge the natural history and usually benign nature of febrile convulsions. Caretakers should be instructed on how to manage their child should another seizure occur. Encourage the caregivers to move the child from any position that places him/her at harm. Caregivers should be advised to maximize the airway by chin lift or jaw thrust maneuvers, which should be demonstrated, and to place the child in a left lateral decubitus position. They should be encouraged to observe the length and time of the seizure. Indications for EMS should be reviewed.

Compliance is likely to be improved when the caregivers are given explicit written instructions that are verbally reinforced by both the physician and the nursing staff.[111] The instructions should indicate the preferred dose and frequency of antipyretic therapy for the current febrile illness. Indications for repeat examination should be discussed. Caregivers should be encouraged to have a physician encounter in the subsequent days following the current event.

Complete the Medical Record

Following the encounter with a febrile child, the medical record should be completed. Document the history and physical exam as well as the decision-making process for the child in the ED. Record repeated checks on the patient and document improvement or any worsening of their condition. Indicate a diagnostic impression and the likely underlying cause of the febrile illness. Note a discussion of all results and treatments with the caregivers, as well as discharge instructions.

Conclusion

Simple febrile seizures are a common event in childhood and usually have a benign course. Rarely, serious extracranial infections precipitate a febrile seizure. A careful history and physical exam is usually all that is needed. A home-going disposition is likely for patients with febrile seizures, yet admission for continued observation may be prudent for patients who are at higher risk for adversity. Pragmatic evaluation should be targeted based on clinical concerns and disposition based on clinical and social factors. The vast majority of children with febrile seizures will have a benign course.

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CME Questions

1. The peak incidence of febrile seizures (FS) occurs at approximately what age?
   A. 18 months
   B. 10 years
   C. 6 months
   D. 3 months

2. FS occur most commonly in which of the following seasons?
   A. Summer
   B. Winter
   C. Spring
   D. Fall

3. In the patient who is actively seizing, clinicians should maximize control of the airway using which of the following?
   A. Chin lift
   B. Jaw thrust
   C. Lateral decubitus positioning
   D. All of the above

4. When obtaining patient history about a FS, which periods of time should be differentiated during discussions with caregivers?
   A. Pre-seizure
   B. The seizure itself
   C. Post-seizure
   D. All of the above

5. In FS, clues to a toxic child include which of the following?
   A. Signs of poor perfusion or lethargy
   B. Altered motor tone
   C. Abnormal cry
   D. Abnormal respiratory rate or pulse
   E. All of the above

6. Physical exam findings in FS that should prompt further evaluation and a search for a more serious source of infection include which of the following?
   A. Prolonged post-ictal lethargy
   B. Focal neurologic deficits
   C. Todd paralysis
   D. Signs of increased intracranial pressure
   E. All of the above

7. Simple febrile seizures comprise what percentage of febrile seizures?
   A. 75%
   B. 25%
   C. 5%
   D. 10%

8. According to the article, which of the following is the most clearly defined mechanism by which febrile illness causes convulsions?
   A. Gene mutations
   B. No single mechanism has been proven in multiple studies, indicating a likely polymorphic etiology of febrile seizures
   C. Respiratory alkalosis
   D. Direct viral mediated affects on the brain

9. Extracranial serious bacterial infections (SBI) include which of the following?
   A. Occult bacteremia
   B. Pneumonia
   C. Osteomyelitis and pyarthrosis
   D. Pyelonephritis and enteric pathogens
   E. All of the above

10. Factors that place children with febrile seizures at high risk for acute bacterial meningitis (ABM) include which of the following?
   A. Physician visit within the previous 48 hours
   B. Focal seizure
   C. Abnormal findings on neurologic exam
   D. All of the above

Answers: 1. A; 2. B; 3. D; 4. D; 5. E; 6. E; 7. A; 8. B; 9. E; 10. D

In Future Issues: **Viral Myocarditis**

PEDIATRIC Emergency Medicine Reports
The Practical Journal of Pediatric Emergency Medicine

Children with Febrile Seizures

Emergency Physician Responsibilities for the Febrile Seizure Patient

- ❑ Provide supportive care
- ❑ Allay caregiver anxiety
- ❑ Extract patient history
- ❑ Perform physical examination
- ❑ Categorize the seizure
- ❑ Consider precipitating causes
- ❑ Determine the likelihood of an intracranial infection
- ❑ Determine likelihood of an extracranial, serious bacterial infection (SBI)
- ❑ Establish a differential diagnosis
- ❑ Determine the need for medications
- ❑ Determine if diagnostic studies are warranted
- ❑ Share the natural history with the caregiver
- ❑ Know prophylactic options
- ❑ Determine the disposition
- ❑ Provide specific discharge instructions
- ❑ Complete the medical record

First-line Benzodiazepines for the Management of Febrile Seizures

MEDICATION	DOSE	ROUTE
Lorazepam	0.1 mg/kg	IV/IM
Diazepam	0.3 mg/kg	IV/IM
	0.5 mg/kg	Rectal
Midazolam	0.1 mg/kg	IV
	0.15 mg/kg	IM
	0.2 mg/kg	Intranasal
	0.3 mg/kg	Buccal

Adapted from references 49, 50, 52, 53, 55, and 56

Risk Factors for Febrile Seizures

FIRST FS	RECURRENT FS	EPILEPSY RISK
Family history, 1st degree	Family history, 1st degree	Family history of epilepsy
Developmental delay	Onset < 18 months	Neurologic abnormality
Maternal smoking	Lower temperature around 38° C	Short fever duration before seizure
Daycare attendance	Short fever duration (<1 hour) before seizure	Complex seizures
Infertility treatment		
Prematurity		

Adapted from references: 1, 92

Features that Increase the Risk for Acute Bacterial Meningitis in Patients with Apparent Febrile Seizure

GENERAL HISTORY	SEIZURE PATTERN	PHYSICAL EXAMINATION
Age ≤ 12 months	Focal seizure	Blunted response to overture
Exposure to invasive disease	Motor, speech, or vision deficit	Poor perfusion
Ill at least 3 days	Multiple seizures	Generalized petechiae
Physician visit in antecedent 48 hours	Prolonged seizure	Altered motor tone
Documented bacteremia	Field or ED anticonvulsants	Abnormal cry
On antibiotics for extracranial infection	Prolonged post-ictal phase	Hard to console
Immunocompromised		Inability to fix and follow with eyes
Neurosurgical procedures, hardware		Nuchal rigidity
Penetrating head trauma		Full fontanel
		Focal neurologic deficit

Differential Diagnosis of Febrile Seizures

MASQUERADING AS SIMPLE	MASQUERADING AS COMPLEX	OVERLAPPING FEATURES
Viral meningitis	Hemiplegic migraine	Occult closed head injury
Shigellosis	Moya moya disease	Acute demyelinating disease
Salicylism	Brain abscess	Periarteritis nodosa
Lead intoxication	Viral encephalitis	Systemic lupus
Neuroleptic malignant syndrome	Acute bacterial meningitis (ABM)	CNS tumor with bleed
Antidepressant overdose		

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