BMJ Best Practice

Febrile seizure

Straight to the point of care



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Summary

Febrile seizures are usually self-limiting; increased risk of developing epilepsy is low except in a small number of cases.

Most febrile seizures resolve spontaneously and quickly, and do not require acute or long-term anticonvulsant treatment.

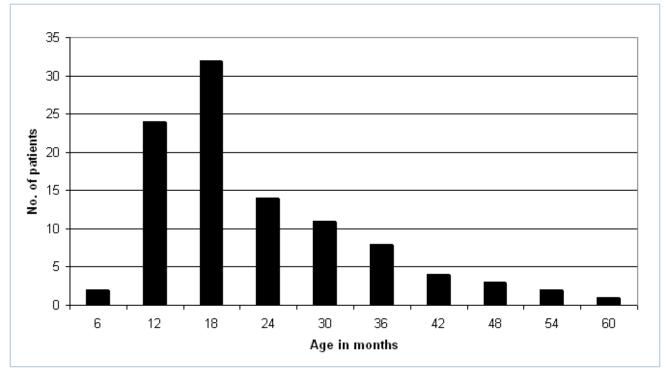
Definition

The American Academy of Pediatrics defines a febrile seizure as a seizure occurring in a febrile child (temperature ≥100.4°F or 38°C) between the ages of 6 and 60 months who does not have an intracranial infection, metabolic disturbance, or history of afebrile seizures.[1] [2] The first occurrence is usually before 3 years of age but is infrequent in children under 6 months. Febrile seizures may be classified as simple or complex depending on clinical features, duration, and recurrence.

The 2006 report by the International League Against Epilepsy Task Force on Classification and Terminology of Epilepsy and Epileptic Syndromes proposed a change in terminology and the omission of the words "convulsion" and "convulsive." They suggested that the term "febrile convulsions" be replaced by "febrile seizures."[3] Further changes in 2017 included replacing the term "benign" with "self-limiting."

Epidemiology

Febrile seizures are common in childhood. The cumulative incidence is estimated to be between 2% and 5% in the US and Western Europe, between 6% and 9% in Japan, and 14% in India and Guam.[4] In Asia, the most common cause is influenza A, especially prevalent in epidemics.[10] [11]



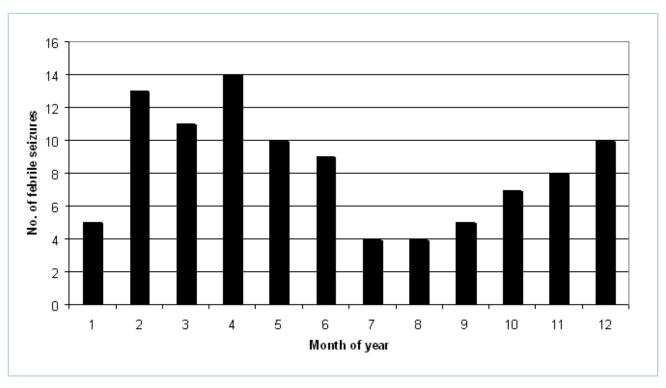
Age of occurrence of febrile seizures in 100 consecutive children treated in a university-affiliated tertiary care hospital: maximum frequency between ages 12 and 18 months, with a rapid decline after 24 months of age

Graph created by John J. Millichap, MD; used with permission

Most population-based studies report a sex ratio of 1.6 boys to 1 girl.[7] [12] The wide geographic distribution of case reports in the literature suggests children of all races are affected. A socioeconomic factor has not been demonstrated.

Genetic susceptibility, young age, immaturity of the central nervous system, and environmental factors are important as they are modifiers of the threshold convulsive temperature. Autosomal-dominant, -recessive, and polygenic modes of inheritance have been described and several genetic loci identified.

Seasonal, circadian, geographic, electrolyte, and nutritional variables (i.e., iron and zinc deficiency) also have roles in susceptibility.[11] [13]



Seasonal occurrence of febrile seizures in 100 consecutive children treated in a university-affiliated tertiary care hospital: maximum frequency in spring and winter; lowest frequency in summer months Graph created by John J. Millichap, MD; used with permission

Etiology

Viral infections triggering fever are the most common cause, with bacteremia as an infrequent cause.[10] [11] [14] [15] [16]

A retrospective cohort study of more than 900 febrile seizures showed the risk of developing febrile seizures is similar with influenza, adenovirus, or parainfluenza and is lower with respiratory syncytial virus or rotavirus. The type of viral infection was not important in predicting complex features or future recurrences.[17] The frequency of these infections was not significantly different in a control group of patients with fever but without seizures.

A prospective multicenter study of children with prolonged febrile seizures found human herpesvirus (HHV)-6 infection to be commonly associated with febrile status epilepticus; HHV-7 infection was less frequently associated, but together they accounted for one third of febrile status epilepticus.[18]

The International League Against Epilepsy described a monogenic etiology that may cause a spectrum of mild to severe epilepsies, such as SCN1A mutations, which are associated with Dravet syndrome and genetic epilepsy with febrile seizures plus (GEFS+). There is an increasing tendency to define newly described epileptic disorders primarily in genetic terms, with clinical features being linked to genotypes.[19] In the future, the diagnosis of febrile seizures may be influenced by a greater understanding of the genetic epilepsies.[20]

Pathophysiology

Febrile seizures are dependent upon a threshold temperature and this seems to vary from one individual to another.[12] [21] [22] Age plays an important role in the susceptibility of febrile seizures; the risk of recurrence of seizure declines with growing older. If there is an individual temperature threshold level above which a febrile seizure will develop, this threshold is influenced by age: as the child grows older, the higher the threshold, the lower the risk.[23] The minimum temperature increase required to diagnose fever varies according to scientific societies and measuring methods, and has changed over time. Fever is generally defined as a temperature of ≥100.4°F (38.0°C).[1]

A specific neurotropism or central nervous system-invasive property of certain viruses (e.g., human herpesvirus-6 [HHV-6], influenza A), and bacterial neurotoxin (*Shigella dysenteriae*) has been implicated, but the evidence is inconclusive.[11] In some cases, HHV-6 may invade the brain during the acute viremic phase of exanthem subitum. Exanthem subitum, otherwise known as roseola or sixth disease, is a febrile illness often accompanied by a rash, lymphadenopathy, and gastrointestinal or respiratory symptoms. Seizure recurrence may be associated with reactivation of the HHV-6 virus. The definition of febrile seizure may need to be modified to include a mild encephalitis or encephalopathy in these cases. The type - simple or complex - may be related to a viral neurotropism or to the severity of a cytokine immune response to infection.[24]

Classification

Febrile seizures may be classified as simple or complex depending on clinical features, duration, and recurrence.

Simple febrile seizures are usually defined as primary generalized seizures lasting less than 15 minutes, resolving spontaneously, and not recurring during a 24-hour period.[1] [2] [4] Results of the FEBSTAT study, a prospective multicenter study of 158 children with a first febrile seizure, have suggested that an upper time limit of 10 minutes' duration may be more appropriate for the definition of simple febrile seizures.[5] The widely accepted definition of simple febrile seizures still includes a seizure duration of up to 15 minutes; however, the majority of febrile seizures last less than 10 minutes.[4]

Complex febrile seizures are defined by one or more of the following features: a focal onset or focal features during the seizure, prolonged duration (greater than 10-15 minutes), recurrence within 24 hours or within same febrile illness, or incomplete recovery.[1] [2] [4] [6]

Between 9% and 35% of all first febrile seizures are complex.[6]

Case history

Case history #1

A previously healthy and developmentally normal 18-month-old boy presents to the emergency department by ambulance after his parents witnessed a seizure. The parents report the boy had a febrile illness with mild upper respiratory symptoms and they treated him with acetaminophen at home. The child then began to have frequent jerking movements of all limbs. The temperature was 103.1°F (39.5°C). The parents called 911, the child was taken to the emergency department. The jerking stopped

after approximately 5 minutes. Afterward, the child was sleepy but responsive to verbal stimulation. Examination revealed a diffuse erythematous maculopapular rash and a normal mental and neurologic status.

Case history #2

A 10-month-old girl is brought to the emergency department with a history of recurrent right arm and leg jerking followed by prolonged sleepiness. The parents report a 2-day history of fever with chest congestion and irritability. The child is admitted to the hospital for neurologic evaluation.

Other presentations

Febrile seizures before 6 months of age in a child with a relatively low fever are atypical and require a full investigation to exclude acute bacterial meningitis or other CNS pathology. Another atypical presentation is a child with a prolonged focal (complex) febrile seizure who has Todd paralysis (transient hemiparesis) on recovery of consciousness. In one prospective series of 95 patients with febrile seizure, 2% had Todd paralysis.[7] Febrile status epilepticus is a prolonged or recurring seizure with fever and without recovery of consciousness between episodes. Classically, the duration is 30 minutes or more; some include seizures of shorter duration (10 minutes or more). Tonic-clonic generalized status is most common. In a large prospective, controlled study, patients with febrile seizure status were more likely to have neurologic abnormalities, a history of neonatal seizures, and a family history of epilepsy.[8] A prospective multicenter study of children with febrile status epilepticus (FEBSTAT study) found a median age of 1.3 years, and seizures that were most often focal, partial, and long, lasting a median of 68 minutes.[9] Febrile status epilepticus was frequently the first febrile seizure, and status was unrecognized in the emergency department.

Approach

The diagnosis is made through clinical assessment; however, as ruling out meningitis often drives the approach, related tests may take precedence. Infants who present with a suspected febrile seizure under the age of 6 months require particularly careful medical evaluation.

History

The patient tends to be young (age 3 months to 5 years, most commonly 12 to 24 months), male, and presenting with a fever that is followed soon after by loss of consciousness and generalized clonic movements and/or tonic stiffening. The seizure is commonly short in duration (3 to 5 minutes) and recovery of consciousness rapid, without sequelae. The degree of fever is generally high. Often there is a family history of febrile seizures. A seizure that is focal, lasts >15 minutes, or is repeated within a 24-hour period is classified as a complex febrile seizure.

Fever etiology

A viral infection is generally suspected, with upper respiratory tract symptoms, otitis media, or gastroenteritis. A typical erythematous maculopapular rash of exanthem subitum (roseola, sixth disease), human herpesvirus-6 infection, or an epidemic of influenza A may define the cause more specifically. In practice, the virus is not usually identified. Rapid simple methods of viral detection are emerging that may allow early diagnosis and the use of antiviral agents. Bacteremia is rare, but meningitis should always be considered.[41]

Physical signs consistent with diagnosis

Physical signs are as follows: extracranial infection and fever (e.g., upper respiratory infection, otitis media, gastroenteritis); rapid recovery of consciousness after seizure (within 30 minutes); and absence of nuchal rigidity and focal neurologic abnormalities.

Exclusion of meningitis

Lumbar puncture (LP) is indicated to rule out meningitis or encephalitis if: presence of suspicious symptoms and signs (e.g., bulging fontanelle, nuchal rigidity) and if age is <12 months (signs of meningitis are often absent in this age group); a focal, prolonged, or multiple seizure occurs within 24 hours with prolonged impairment of consciousness; or there is history of persistent irritability or lethargy, or pretreatment with oral antibiotics (prior antibiotic treatment can mask meningitis, and therefore performing a LP should be given consideration in this setting).[1] There is no evidence, however, to support routine LP in all children admitted with a simple febrile seizure, especially when typical clinical signs of meningitis are lacking.[42] [43]

A meta-analysis showed that in children with an apparent simple febrile seizure, the average prevalence of bacterial meningitis was 0.2% (range 0% to 1%). The pooled prevalence of bacterial meningitis among children with an apparent complex febrile seizure was 0.6% (95% CI 0.2 to 1.4).[44] Another multicenter cohort study of children presenting with a complex febrile seizure found rates of bacterial meningitis and herpes simplex encephalitis were 0.7% and 0%, respectively.[45]

According to the American Academy of Pediatrics (AAP), the potential risks associated with LP are outweighed by the benefits. It should be noted that the AAP proposed modifications of the 1999 guidelines, in response to critical appraisal in the literature, and these have generally been accepted by the profession.[1] Some authorities, especially specialists in pediatric emergency medicine, have

questioned the justification for recommendations based on age. Some difference of opinion remains regarding LP in younger children with suboptimal immunization status for their age. UK guidelines state that the experience of the practitioner and the infant's age (<1 year) are important in judging the need for LP.[46] The AAP recognizes that clinical skills vary between examiners and recommends a conservative approach with emphasis on the diagnostic value of the LP. A previously normal result on LP does not rule out meningitis in a child whose clinical condition deteriorates subsequently. In practice, the AAP guidelines are not strictly followed and should not replace clinical judgment.[2] [47] [48]

Tests

A simple febrile seizure does not usually require further evaluation such as electroencephalography, neuroimaging, or other studies.[1] [49] [50] [51]

However, meningitis should be considered in the differential diagnosis for any unwell febrile child.[52] [53]

Lumbar puncture is the key test to rule out meningitis or encephalitis. An electroencephalogram (EEG), computed tomography scan, or magnetic resonance imaging (MRI) scan is unnecessary after a first febrile seizure.[1][49] [50] [51] [54]

- MRI is not indicated in a child with simple febrile seizure because it does not aid diagnosis or treatment and is associated with risk from sedation.[1] [50] However, MRI should be considered in children with complex febrile seizures, an atypical history with abnormal developmental history, or abnormal neurologic exam.
- The role of EEG in the workup of febrile seizure remains controversial.[55] Do not routinely use
 EEG for neurologically healthy children after a simple febrile seizure, because it can increase
 caregiver and child anxiety without altering the outcome or course of treatment.[1] [51] One
 Cochrane review found no evidence to support or refute the use of EEG and its timing after
 complex febrile seizures among children under the age of 5 years.[56] [57] A neurologist should be
 consulted in these cases.
- CT does not aid diagnosis or treatment and is associated with a slightly increased long-term risk of cancer.[50]

Laboratory evaluations

Serum electrolytes, complete blood count, and blood glucose tests are not routinely recommended.[1] [49] However, these tests may be required to determine the cause of fever.[1] Check capillary blood glucose for hypoglycemia. If there is prolonged postictal impaired consciousness or vomiting and ketosis, electrolyte levels may be indicated. Calcium, phosphorus, and magnesium levels are unnecessary. Viral studies may be useful in patients with complex febrile seizures and symptoms of encephalitis or encephalopathy.

History and exam

Key diagnostic factors

febrile illness (common)

• A body temperature of 100.4°F (38°C) or above, taken immediately before or at seizure onset, is often regarded as a significant fever in the diagnosis, but some children may have febrile seizures at lower temperatures.[1] [21] [65]

seizure (common)

- Usually accompanied by a high temperature and soon after with loss of consciousness and generalized tonic-clonic seizure lasting <15 minutes.
- Consciousness is recovered quickly, within 30 minutes.
- · No sequelae.
- Less commonly, some seizures are prolonged, focal, or multiple, and recovery of consciousness is delayed.

Other diagnostic factors

normal postictal exam (common)

· Neurologic exam normal postictally.

Risk factors

Strong

temperature elevation

- The risk almost doubles for each degree above 100°F (37.8°C).[22] [23]
- The threshold convulsive temperature varies with the individual, age, and genetic and environmental factors.

young age

- Incidence is rare under 6 months and after the fifth birthday; 60% of first seizures occur by the second birthday, 80% by the third, and 95% by the fifth.[12]
- May be explained by age-related susceptibility and exposure to certain viral infections and changes in brain maturation.[12]

family history of febrile seizures

- Family and twin studies confirm a strong genetic component underlying the risk for febrile seizures.[25]
 Genes have been identified for some epilepsy syndromes, but specific genes for "simple" or self-limited febrile seizures have been difficult to identify.[26]
- The most consistently identified risk factor for febrile seizure is the presence of a close family history (within first-degree relatives) of febrile seizure. The more relatives affected, the greater the risk.
 In cohorts of children with febrile seizure, the risk that siblings will have a febrile seizure is 10% to 45%.[6]

viral or bacterial infection outside the central nervous system

- Bacterial infection (e.g., otitis media) is sometimes the source of fever.
- Certain viruses (i.e., human herpesvirus-6 and influenza A) are associated with a relatively high incidence of febrile seizures.
- Viral infections occur with equal frequency in febrile patients with or without seizures, and factors other than the virus may explain the tendency to have a seizure.
- Multiple factors, including proinflammatory cytokines and immune response, may be involved, temperature elevation being the essential trigger.[11] [24] [27]

Weak

male sex

• Boys are affected more than girls, with a ratio of 1.6 to 1.[7]

vaccinations

- The measles, mumps, and rubella (MMR) vaccine accounted for 25 to 34 cases per 100,000 children and the diphtheria, tetanus, and pertussis (DTP) vaccine accounted for 6 to 9 cases per 100,000 children.[28]
- Highest risk on the day of vaccination with DTP and at 7 to 14 days after vaccination with MMR, coincident with a febrile period.[28] [29]
- The risks declined significantly with the introduction of acellular pertussis vaccine (1997-1998), whereas frequency related to MMR showed no significant change between 1995 to 1996 and 1998 to 2001.[30]
- MMR-varicella combination vaccine is associated with a greater risk of seizures than MMR and varicella vaccines administered separately.[31]
- Vaccination with the combined diphtheria-tetanus toxoids-acellular pertussis-inactivated poliovirus-Haemophilus influenzae type b (DTaP-IPV-Hib) vaccine is associated with a small increase in the risk of febrile seizures on the day of administration at 3 and 5 months of age, but not when the vaccine is given at 12 months of age.[32]
- Risk of fever and seizure following a measles-containing vaccine is significantly lower when administered at 12 to 15 months than at 16 to 23 months of age.[33]

prenatal exposure to nicotine

- Slightly increased risk in children if mothers smoked 10 or more cigarettes a day during pregnancy.[34]
- No documented association with maternal alcohol and coffee consumption.[34]

iron deficiency

- Iron insufficiency has a possible role in the occurrence of first seizures.[35]
- Mean ferritin levels were significantly lower in affected children than in controls (29.5 versus 53.3 micrograms/L; P = 0.0001).[35] Lower levels of hemoglobin and mean corpuscular volume were not significantly different.
- Two meta-analyses suggested that iron-deficiency anemia is associated with an increased risk of febrile seizures in children.[36] [37]

complications of pregnancy, labor, and delivery

• In a large pediatric population followed prospectively, complications of labor and delivery were not important risk factors.[38]

- Fetal growth retardation is associated with an increased risk of febrile seizures.[39]
- In a community-based prospective case-control study, prenatal and perinatal risk factors were
 compared. There were no differences between cases and controls in factors occurring during delivery
 such as occurrence of acute or elective cesarean section, signs of fetal distress in amnion fluid,
 abnormalities of fetal heart rate, or duration of delivery. Perinatal asphyxia was uncommon and there
 was no difference between cases and controls.[40]

Tests

1st test to order

Test	Result	
diagnosis is clinical	seizures associated with	
 Tests may be required to identify the source of fever. 	fever	

Test to avoid

Recommendations	Rationale
head CT • Do not order head CT in a child with febrile seizure.[1] [50]	 CT does not aid diagnosis or treatment and is associated with a slightly increased long-term risk of cancer.

Other tests to consider

Test	Result
 Iumbar puncture Indicated to rule out meningitis or encephalitis if: presence of suspicious symptoms and signs (e.g., bulging fontanelle, nuchal rigidity) and if age is <12 months; a focal, prolonged, or multiple seizure occurs within 24 hours with prolonged impairment of consciousness; or there is history of persistent irritability or lethargy, or pretreatment with oral antibiotics. 	normal cells, protein, and glucose
 viral studies Viral studies may be useful in patients with complex febrile seizures 	may be positive
and symptoms of encephalitis or encephalopathy. blood culture • Bacteremia is rare, but meningitis should always be considered.	bacteremia may be present
 Bacteremia is rare, but meningitis should always be considered. EEG The role of electroencephalography (EEG) in the workup of febrile seizure remains controversial. [55] Do not routinely use EEG for neurologically healthy children after a simple febrile seizure, because it can increase caregiver and child anxiety without altering the outcome or course of treatment. [1] [51] There is no evidence that an EEG can be used to predict whether a child will develop epilepsy after a simple febrile seizure. Also, development of epilepsy cannot be prevented by knowledge of EEG findings. [66] However, acute EEG may have a role following status epilepticus. The FEBSTAT study performed baseline EEGs within 72 hours of an episode of febrile status epilepticus. Review of the baseline EEGs showed a focal EEG slowing or attenuation in a substantial proportion of children. The slowing and attenuation are highly associated with MRI evidence of acute hippocampal injury. These findings may be a sensitive and readily obtainable marker of acute injury associated with febrile seizure epilepsy. [56] Recurrent simple or complex febrile seizures also do not justify an EEG, as it is of no use in identifying a structural abnormality or in predicting recurrent febrile seizure or the development of epilepsy. [67] EEG should be considered in all children with complex febrile seizures that recur with afebrile convulsions, or in children who have recurrent febrile seizures and also exhibit developmental delays or abnormal neurologic signs and symptoms. [68] One Cochrane review found no evidence to support or refute the use of EEG and its timing after complex febrile seizures among children under the age of 5 years. [57] Focal EEG slowing or attenuation are present in EEGs obtained within 72 hours following febrile status epilepticus in a substantial proportion of children. [56] Neurologic consultation is needed. 	possible focal EEG slowing or attenuation following febrile status epilepticus
 brain MRI Usually normal; may show hippocampal edema or sclerosis with complex, prolonged, and focal febrile seizure.[56] [69] [70] MRI is not indicated in a child with simple febrile seizure because it does not aid diagnosis or treatment and is associated with risk from codding. [11, [50] However, MRI should should be considered.] 	may show acute hippocampal edema or chronic hippocampal sclerosis

from sedation.[1] [50] However, MRI should should be considered

Test	Result
in children with complex febrile seizures, an atypical history with abnormal developmental history, or abnormal neurologic exam.	
serum sodium	may be low (<130 mEq/L)
 Hyponatremia may increase the risk for multiple seizures during the same febrile illness.[71] Despite these and other similar reports, the American Academy of Pediatrics does not recommend routine serum electrolytes after a first simple febrile seizure.[1] [49] However, serum electrolytes may be of use in children with complex febrile seizure. 	
СВС	variable
 Not routinely recommended, but may be required to determine the cause of fever.[1] [43][49] 	
capillary blood glucose	usually normal
 A capillary blood glucose test should be performed on all children who present with a seizure to exclude hypoglycemia. 	
serum glucose	usually normal
 Usually normal.[1] Not indicated routinely, but may be useful with complex febrile seizures, prolonged postictal obtunded consciousness, or vomiting and ketosis.[1] 	
iron studies	may reveal deficiency
 Consider testing if clinically indicated or other blood tests are being performed.[72] 	

Differentials

Condition	Differentiating signs / symptoms	Differentiating tests
Acute bacterial meningitis	 Persistent irritability and lethargy, prolonged postictal obtunded consciousness, skin rash, bulging fontanelle, and nuchal rigidity. 	Typical cerebrospinal fluid abnormalities are pleocytosis, elevated protein, low glucose level, and positive culture.
Viral meningitis	Fever, headache, neck stiffness are common. Nausea, vomiting, and photophobia can also occur.	 Cerebrospinal fluid: lymphocytic pleocytosis. Glucose is normal or high. Gram stain and bacterial culture are negative; viral culture and polymerase chain reaction may be positive.
Viral encephalitis	 Prodromal upper respiratory symptoms with fever and malaise, followed by headache, stiff neck, and seizure. Skin rash also common. 	 Lumbar puncture may show pleocytosis and increased protein but is sometimes normal. Culture is negative for bacteria. Results of viral studies are positive (i.e., herpes simplex, varicella).
Acute encephalopathy	Viral prodrome, vomiting, followed by profound impairment of consciousness and seizures. Toxins include aspirin (Reye syndrome).	 Lumbar puncture may reveal elevated cerebrospinal fluid pressure, increased cell count, and protein, with moderately decreased glucose. Bacterial cultures are negative. An elevated cerebrospinal fluid/serum albumin ratio indicates an impaired bloodbrain barrier and is the earliest sign of acute viral encephalopathy.[73] Liver enzymes and blood ammonia may be elevated. Low blood glucose may be present. Electroencephalographic abnormalities are variable but are of prognostic significance. MRI abnormalities may include bilateral thalamic necrosis, white matter lesions, and brain edema. MRI may also be normal.

Condition	Differentiating signs / symptoms	Differentiating tests	
		Viral studies may be positive (e.g., influenza A).	
Epileptic seizure	Afebrile seizure.	Electroencephalogram shows paroxysmal epileptiform discharges (e.g., spikes, spike and slow wave).	
Generalized epilepsy with febrile seizures plus (GEFS+)	 Familial epilepsy syndrome in which patients can have a classic febrile seizures that persist beyond the age of 5 years (i.e., FS+), and/or epilepsy. Both genetic and environmental factors have been shown to contribute to the pathogenesis of febrile seizure and GEFS+.[74] Seizures cease by midchildhood (median age 11 years). An evolving composite of many syndromes, with shared genetic susceptibility.[75] 	Genetic tests show links to chromosomes 2q24, 19q13, and 5q31, an autosomal-dominant inheritance with 50% penetrance.	
Hot water epilepsy (HWE)	 The diagnosis is made by history. Seizures are usually focal and are precipitated by bathing or pouring hot water (104°-122°F [40°-50°C]) over the head. Most common in India and Turkey. Not age-dependent, but males predominate 3:1. Only 7% have history of febrile seizures. Family history positive for epilepsy in 22%, and for HWE in 7%.[76] 	Interictal electroencephalogram shows temporal spikes.	
Breath-holding spells	 Afebrile infant, with an apneic attack, cyanosis, loss of consciousness, and short generalized episodes of jerking of extremities after a crying spell. The breath is held in expiration. Onset is 6 to 18 months of age, similar to that of febrile seizures. 	 Electroencephalogram is usually normal and the attacks do not predispose to epilepsy.[77] CBC and serum ferritin may uncover an associated iron deficiency anemia.[36] 	

Condition	Differentiating signs / Differentiating tests symptoms		
	 Some noncyanotic, pallid breath-holding spells result from vagal stimulation after an unpleasant, unexpected stimulus. These are associated with cardiac asystole and are accompanied by syncope or anoxic seizure. 		
Dravet syndrome: severe myoclonic epilepsy of infancy	 Intractable epilepsy, resembling febrile seizure disorder in first year. Seizure onset early, recurrent (>5), prolonged, often focal and clonic. There is evidence that vaccination triggers the onset of febrile seizures in one third of patients with Dravet syndrome.[78] 	SCN1A mutation analysis positive.[79]	

Approach

Control of the seizure is the first goal in treatment. During a witnessed seizure, the patient should be protected from physical injury. Additionally, airway, breathing, and circulatory assessment and support are vital. Most seizures will stop spontaneously within a few minutes, and anticonvulsant therapy is not needed. Body temperature should be reduced to relieve discomfort.

Although many children presenting to the hospital with simple febrile seizures are managed appropriately, a large number are over-investigated and overtreated, based on the clinical experience of the treating doctor.[42] [82] Clinical acumen remains the most important tool for identifying children with seizures who are candidates for a more elaborate diagnostic evaluation.[83] Recognizing the pattern of a simple febrile seizure in young children is important to limit interventions and to reassure parents.[84]

First simple febrile seizure

- Most causative infections are viral and do not require antibiotics.[11] [41]
- Antipyretic agents are ineffective for preventing recurrences of febrile seizures and for lowering body temperature in patients with a febrile episode that leads to a recurrent febrile seizure.[46] [85] [86] [87] Antipyretics facilitate heat loss, but are not absorbed sufficiently rapidly to affect the height of the temperature above the individual's temperature threshold that leads to seizure.[86]
- Recommendations differ; ibuprofen is long-acting and is often the preferred antipyretic agent. [88]

Febrile illness and one prior seizure

There is no evidence of the effectiveness of antipyretics in preventing future febrile seizure.[42] [81]

Early administration of an antipyretic and oral diazepam at first sign of fever or seizure activity is not recommended in the American Academy of Pediatrics (AAP) guidelines for simple febrile seizures, largely due to the fact that although antipyretics facilitate heat loss they are not absorbed sufficiently rapidly to reduce the peak temperature, and the potential toxicities associated with anticonvulsant agents outweigh the minor risks associated with simple febrile seizures.[2] However, a systematic review with meta-analysis concluded that treatment remains controversial and depends on appropriate judgment and the experience of the physician.[89] Another systematic review concluded that, although statistically significant benefits have been shown for some anticonvulsants in preventing seizure recurrence, there was a high prevalence of adverse events and the quality of the evidence was low.[87] The number needed to treat to prevent one seizure over 1 to 2 years was 16, which was considered to be clinically unimportant in the context of associated adverse events. Antipyretic intervention does not affect the recurrence rate of subsequent febrile seizures, and there is no indication for initiation of chronic anticonvulsant drugs for simple febrile seizures.[81] [90]

Complex febrile seizure

Patients with complex febrile seizures have episodes of either focal, prolonged (lasting >15 minutes), or multiple seizures in 24 hours. Treatment may include administration of ibuprofen until the fever abates. Additionally, diazepam can be given rectally and repeated if the seizure activity continues. Furthermore, the use of rectal diazepam will reduce the risk of febrile seizure recurrence during an illness, but benefits and potential toxicity should be carefully considered.[87] [91] Complex febrile seizures have a relatively guarded prognosis compared with simple febrile seizures, and the 2008 AAP guidelines for treatment of simple febrile seizures do not apply.

Initial management of infants and young children with complex febrile seizures is often at the primary or secondary level, but there should be a low threshold for referral to a pediatrician (secondary/tertiary level) for evaluation of the underlying cause and further management.[81] [92]

Febrile status epilepticus

- Febrile status epilepticus may be defined as a prolonged seizure or recurrent brief seizures without complete recovery of consciousness. The duration criterion is controversial, but preparations for implementation of a full status epilepticus protocol should begin after failure of initial benzodiazepine treatment.[93] [94]
- The FEBSTAT study, a prospective multicenter study of febrile status epilepticus, found that prolonged seizures occurred in very young children and were most often focal, partial, and long, lasting a median of 68 minutes.[9] Febrile status epilepticus was frequently the first febrile seizure, and status was unrecognized in the emergency department. Further analysis of the results from the study found that human herpesvirus (HHV-6 and HHV-7) accounted for around one third of febrile status epilepticus, and that febrile status epilepticus rarely causes cerebrospinal fluid (CSF) pleocytosis; thus, CSF pleocytosis should not be attributed to febrile status epilepticus but should be considered evidence of probable meningitis.[18] [95]
- Ambulance treatment of febrile seizures. In one prospective study of children presenting to the emergency department with prolonged febrile seizures (>15 minutes), of those receiving rectal diazepam in the ambulance only 11% responded, compared with 58% of patients treated with intravenous diazepam.[96]
- Status epilepticus should be managed according to local/national guidelines.

Anticonvulsant treatment

- Upon assessment of a patient with a seizure continuing >5 minutes, a dose of rectal diazepam is given. Then, if the seizure does not abate in 10 minutes, another dose is given.
- If these 2 doses of rectal diazepam fail, one dose of intravenous fosphenytoin is given.
- If the seizure still persists, intravenous diazepam is given with a repeat dose at 5 minutes if necessary. Lorazepam is an alternative treatment.
- If the above measures fail, a specialist (pediatric neurologist or pediatric intensivist) should be consulted for the treatment of status epilepticus.
- If emergency hospital services are not readily accessible, diazepam should be provided to be administered in rectal form as soon as possible after the first 5 minutes of seizure activity. Rectal diazepam is the regimen of choice for acute treatment of a prolonged febrile seizure or a cluster of febrile seizures.[97] [98] [99]
- In the US, rectal diazepam is not approved by the Food and Drug Administration for febrile seizures
 or prolonged seizures in children below the age of 2 years. Children <2 years old should be
 admitted to the hospital emergency department for intravenous anticonvulsant therapy.

Prevention of recurrent febrile seizures

- The strongest predictor of recurrence is age <12 to 16 months at the time of the first febrile seizure.[100]
- Other risk factors include family history of febrile seizures in first-degree relative, lower temperature, and shorter duration of fever before initial seizure.[101] The higher the temperature, the higher the risk of recurrence.[23]
- 90% of seizure recurrence occurs within 2 years.
- Febrile seizures recur in approximately 30% of children during subsequent febrile illnesses.[102]

- Prediction of recurrence for individual children is difficult; the mainstay of management is around education of families.[100]
- Patients with 2 or more complex febrile seizures in whom diazepam is ineffective may be considered for long-term anticonvulsant treatment in consultation with a neurologist.
- Prophylactic efficacy with intermittent oral diazepam shows variable results in controlled studies, and is not generally recommended in the current AAP guidelines for simple febrile seizures.[2] [87] However, it may be indicated in certain cases, such as frequent febrile seizure recurrence, low temperature threshold for febrile seizure, and/or parental anxiety.[66]
- A systematic review found no clinically important benefit of antiepileptic and antipyretic treatments
 for the prevention of recurrent febrile seizures in children.[87] Although significant seizure
 prevention was shown for some intermittent anticonvulsant treatments, such as oral diazepam, oral
 clobazam, or rectal diazepam (versus placebo or no treatment), the benefits were not consistent
 over time and there was a high prevalence of adverse events.
- Long-term management requires thorough assessment and risk stratification to devise a
 customized plan for each child, paying attention to the caregiver situation at home and day
 care.[103]

Treatment algorithm overview

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer

Initial		(summary)
febrile status epilepticus		
	1st	consultation with pediatric neurologist or pediatric intensivist

Acute			(summary)
first simple febrile seizure			
	1st	antipyretic	
	adjunct	anticonvulsant	
first complex seizure			
	1st	antipyretic	
	plus	anticonvulsant	

Ongoing		(summary)
febrile illness with prior history of simple seizure or 1 complex seizure		
	1st	antipyretic
	adjunct	prophylactic diazepam
history of 2 or more complex febrile seizures with ineffective diazepam treatment		
	1st	prophylactic anticonvulsant

Treatment algorithm

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer

Initial

febrile status epilepticus

1st consultation with pediatric neurologist or pediatric intensivist

- » Febrile status epilepticus may be defined as a prolonged seizure or recurrent brief seizures without complete recovery of consciousness. The duration criterion is controversial, but preparations for implementation of a full status epilepticus protocol should begin after failure of initial benzodiazepine treatment.[93] [94]
- » Status epilepticus should be managed according to local/national guidelines.

Acute

first simple febrile seizure

1st antipyretic

Primary options

» ibuprofen: children 6 months-12 years of age: 5-10 mg/kg orally every 6-8 hours when required, maximum 40 mg/kg/day

OR

- » acetaminophen: 10-15 mg/kg orally/rectally every 4-6 hours when required, maximum 75 mg/kg/day
- » Simple febrile seizure: generalized, lasts <15 minutes, not repeated in a 24-hour period.
- » Antipyretic agents are ineffective for preventing recurrences of febrile seizures and for lowering body temperature in patients with a febrile episode that leads to a recurrent febrile seizure.[86]
- » Antipyretics, on their own, have not been shown to prevent febrile seizures or their recurrence.[46] [85] [87] They facilitate heat loss, but are not absorbed sufficiently rapidly to reduce the peak temperature.[86] [87]
- » Recommendations differ; ibuprofen acts for longer, and is often the preferred antipyretic agent.[88]

adjunct anti

anticonvulsant

Treatment recommended for SOME patients in selected patient group

Primary options

» diazepam: children <2 years of age: consult specialist for guidance on dose; children 2-5 years of age: 0.5 mg/kg rectally as a single dose, may repeat in 4-12 hours if required; children 6-11 years of age: 0.3 mg/kg rectally as a single dose, may repeat in 4-12 hours if required

Secondary options

» fosphenytoin: infants and children: 15-20 mg/kg (phenytoin equivalents) intravenously as a single dose; consult specialist for further guidance on dose

Tertiary options

Acute

» diazepam: infants and children: 0.1 to 0.3 mg/kg intravenously as a single dose, may repeat after 5-10 minutes if required, maximum 10 mg/dose

OR

- » lorazepam: infants and children: 0.05 to 0.1 mg/kg intravenously as a single dose, may repeat every 10-15 minutes if required, maximum 4 mg/dose
- » If a patient has a seizure lasting more than 5 minutes, an initial dose of rectal diazepam is given. If the seizure does not abate in 10 minutes, another dose is given. The Food and Drug Administration does not approve rectal diazepam for children below the age of 2 years. These children should receive intravenous anticonvulsant therapy.
- » If these 2 doses of rectal diazepam fail, 1 dose of intravenous fosphenytoin is given.
- » If the seizure still persists, intravenous diazepam is given with a repeat dose at 5 minutes. Lorazepam is an alternative treatment.
- » If the above measures fail, a specialist (pediatric neurologist or pediatric intensivist) should be consulted for the treatment of status epilepticus.

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first complex seizure

1st antipyretic

Primary options

» ibuprofen: children 6 months-12 years of age: 5-10 mg/kg orally every 6-8 hours when required, maximum 40 mg/kg/day

OR

- » acetaminophen: 10-15 mg/kg orally/rectally every 4-6 hours when required, maximum 75 mg/kg/day
- » The seizure is prolonged (lasting over 15 minutes), focal, or multiple in 24 hours.
- » Between 9% and 35% of all first febrile seizures are complex.[6]
- » Treatment involves antipyretic until the fever abates.

Acute

plus anticonvulsant

Treatment recommended for ALL patients in selected patient group

Primary options

» diazepam: children <2 years of age: consult specialist for guidance on dose; children 2-5 years of age: 0.5 mg/kg rectally as a single dose, may repeat in 4-12 hours if required; children 6-11 years of age: 0.3 mg/kg rectally as a single dose, may repeat in 4-12 hours if required

Secondary options

» fosphenytoin: infants and children: 15-20 mg/kg (phenytoin equivalents) intravenously as a single dose; consult specialist for further guidance on dose

Tertiary options

» diazepam: infants and children: 0.1 to 0.3 mg/kg intravenously as a single dose, may repeat after 5-10 minutes if required, maximum 10 mg/dose

OR

- » lorazepam: infants and children: 0.05 to 0.1 mg/kg intravenously as a single dose, may repeat every 10-15 minutes if required, maximum 4 mg/dose
- » If a patient has a seizure lasting more than 5 minutes, an initial dose of rectal diazepam is given. If the seizure does not abate in 10 minutes, another dose is given. The Food and Drug Administration does not approve rectal diazepam for children below the age of 2 years. These children should receive intravenous anticonvulsant therapy.
- » If these 2 doses of rectal diazepam fail, 1 dose of intravenous fosphenytoin is given.
- » If the seizure still persists, intravenous diazepam is given with a repeat dose at 5 minutes. Lorazepam is an alternative treatment.
- » If the above measures fail, a specialist (pediatric neurologist or pediatric intensivist) should be consulted for the treatment of status epilepticus.

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Ongoing

febrile illness with prior history of simple seizure or 1 complex seizure

1st antipyretic

Primary options

» ibuprofen: children 6 months-12 years of age: 5-10 mg/kg orally every 6-8 hours when required, maximum 40 mg/kg/day

OR

- » acetaminophen: 10-15 mg/kg orally/rectally every 4-6 hours when required, maximum 75 mg/kg/day
- » Antipyretics improve the child's comfort, but will not prevent seizure recurrence; they facilitate heat loss, but are not absorbed sufficiently rapidly to reduce the peak temperature.[86] [87]
- » Using around-the-clock prophylactic administration of antipyretics has not been shown to affect the incidence of recurrence of febrile seizures, and is not recommended.[104]

adjunct

prophylactic diazepam

Treatment recommended for SOME patients in selected patient group

Primary options

- » diazepam: children >6 months: 0.3 mg/kg orally every 8 hours
- » Oral diazepam is not generally recommended to prevent simple febrile seizure recurrence, due to its potential toxicities.[2] [87] However, it may be indicated in certain cases, such as frequent febrile seizure recurrence, low temperature threshold for febrile seizure, and/or parental anxiety.[66]
- » Prophylactic diazepam may be continued until fever, and therefore risk of seizure, abates.

history of 2 or more complex febrile seizures with ineffective diazepam treatment

1st prophylactic anticonvulsant

- » Long-term anticonvulsant treatment may be considered in consultation with a neurologist.[98]
- » The patient may be slowly weaned off the anticonvulsant after 6 months without seizures.

Primary prevention

Complete prevention through avoidance of fever is impossible given that young children are exposed to numerous common infectious illnesses in childhood. Optimum hygiene in childcare facilities reduces risk of exposure to febrile illness.

Secondary prevention

The occurrence of a febrile seizure may depend, among other factors, on a child's individual seizure threshold temperature.[65] Recurrence may be less likely if the body temperature does not rise above this threshold. Exposure to infectious fevers can be reduced by the observation of optimal hygienic measures (e.g., frequent handwashing) at home and at childcare centers. Immunizations should be current and complete. Vaccinating children at the recommended age may prevent some febrile seizures by protecting children against measles, mumps, rubella, chickenpox, influenza, pneumococcal infections, and other diseases that can cause fever and febrile seizures.[130] Influenza vaccines are indicated, particularly in populations subject to epidemics. The measles, mumps, and rubella (MMR) and MMR-varicella combination vaccines are both associated with an increased risk of seizures.[29] [31] Children at risk of developing a febrile seizure should rather receive MMR and varicella vaccines separately, to reduce risk of recurrence owing to the higher risk of seizures associated with the MMR-varicella combination vaccines.[31] Pharmacologic treatment may be indicated in a small group to minimize recurrence in patients with a history of prior febrile seizures, especially when prolonged, and in status epilepticus. This subgroup is likely to have an underlying genetic epilepsy (i.e., SCN1A mutations). Antiepileptics (phenobarbital and valproic acid) have shown efficacy in preventing febrile seizures, but side effects may outweigh benefits. [98] Antipyretics are useful in treatment of discomfort relating to fever, but they are not effective in prevention.[85] One study from Japan indicated that prophylactic acetaminophen may reduce febrile seizure recurrence following an initial episode. However, methodological considerations mean this study is unlikely to be applicable to other health care systems.[131]

Patient discussions

- A first febrile seizure in a child is a frightening experience. Parents' concerns may continue long after the seizure abates.
- Child should be protected from injury during the seizure.
- Some children have a susceptibility to febrile seizures that resolves before 6 years of age.
- The risk of nonfebrile seizures and epilepsy is small.
- Recurrence is likely, usually within the year, but some preventive measures can be successful.
- If a seizure develops and lasts longer than 3 to 5 minutes, child should be taken to the nearest hospital emergency department.
- · Parents should receive CPR training.

Monitoring

Monitoring

Hospitalization is considered when fever is unresolved, the cause of infection undefined, or follow-up uncertain or difficult. A neurologist should be consulted for patients with complex febrile seizures, prolonged postictal impairment of consciousness, or focal neurologic sequelae.

Parent education is an essential component of the management of care.[87] [129]

Complications

Complications	Timeframe	Likelihood
Todd paralysis	short term	low

Defined as transient hemiparesis after a febrile seizure (usually of complex and focal type).

Neurologic consultation should be obtained, as well as electroencephalogram and magnetic resonance imaging.

nonfebrile seizure variable low

Incidence higher in hospital-based compared with population-based studies.

The risk of developing nonfebrile seizures has been shown to be higher for those who have a family history of epilepsy, a preexisting neurologic abnormality (cerebral palsy), or poor condition at birth (low Apgar scores at 5 minutes).[117]

epilepsy (recurrent nonfebrile seizures) variable low	epilepsy (recurrent nonfebrile seizures)	variable	low
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Epilepsy occurs at a rate of 2% to 6%.[118] [119]

Patients with partial (focal) febrile convulsions showed a trend toward a higher risk of developing epilepsy (45%) than patients with multiple febrile seizures (21%).[120] Epilepsy is not prevented by administration of intermittent or long-term prophylactic anticonvulsant therapy for febrile seizures with epileptiform electroencephalograms.[121]

Between 9% and 35% of all first febrile seizures are complex, and it may be important to establish this at presentation because children with prolonged or multiple febrile seizures are at increased risk of developing unprovoked seizures.[6]

One prospective study of 501 children with a first febrile seizure found a 5.4% risk of occurrence of epilepsy during a 30-month follow-up period. Significant risk factors for subsequent epilepsy included a maternal family history of epilepsy, complex febrile seizure, focal febrile seizure, Todd paresis, short fever duration before febrile seizure, late onset of febrile seizure >3 years, and multiple febrile seizure recurrences. Multiple febrile seizures increased the risk of epilepsy 10 times.[119]

The decision to treat febrile seizures in an attempt to prevent recurrence should be individualized.[66]

focal epilepsy variable low

In patients with intractable focal epilepsy, an association of mesial temporal sclerosis (MTS) is sometimes made with history of prolonged febrile seizures.

There is no evidence of any risk of hippocampal sclerosis or MTS in association with simple febrile seizures.[109]

The association between febrile seizures and temporal lobe epilepsy probably results from complex interactions between several genetic and environmental factors.[122] Clinical and molecular genetic studies suggest that the relationship between febrile seizure and later epilepsy is frequently genetic, and there are a number of syndrome-specific genes for febrile seizure.[123] [124]

MTS, prolonged febrile seizures, and/or a preexisting hippocampal maldevelopment may be a cause of focal epilepsy. If causative, the prevention of complex prolonged febrile seizures is important.

Complications

Timeframe Likelihood

A prospective magnetic resonance imaging study of 329 unselected patients with febrile seizure failed to show any hippocampal injury and concluded there may be no causal relation between febrile seizure and MTS.[6]

Duration of the febrile seizure is an important determinant of later development of epilepsy and epileptiform electroencephalogram.[7] [125]

mesial temporal sclerosis

variable

low

In patients with intractable focal epilepsy, an association of mesial temporal sclerosis (MTS) is sometimes made with history of prolonged febrile seizures.

Specifically, neuronal damage induced by febrile seizures has been suggested as a mechanism for the development of mesial temporal sclerosis, the pathological hallmark of temporal lobe epilepsy. However, the statistical correlation between febrile seizures and temporal lobe epilepsy does not necessarily indicate a causal relationship.[126]

If causative, the prevention of complex prolonged febrile seizures is important.

A prospective magnetic resonance imaging study of 329 unselected patients with febrile seizure failed to show any hippocampal injury and concluded there may be no causal relation between febrile seizure and MTS.[6]

Duration of the febrile seizure is an important determinant of later development of epilepsy and epileptiform electroencephalogram.[7] [125]

behavior and cognitive disorders

variable

low

Measures of cognition, motor ability, and adaptive behavior at 1 month after a first febrile seizure and 1 year later found no difference in performance compared with controls. Factors independent of the febrile seizure that were associated with delay in developmental milestones over time included poor socioeconomic status, TV watching, fewer books, lack of breast feeding, and a febrile seizure complex in type.[127]

Deficits in facial recognition (prosopagnosia) were linked to the size of the hippocampi when tested at 1 year after the prolonged febrile seizure.[128]

Prognosis

Prognosis is generally favorable.[107] [108]

Febrile seizures recur in approximately 30% of children during subsequent febrile illnesses.[102] Most recurrences occur within 2 years. The risk of nonfebrile seizures and epilepsy developing after simple febrile seizures is 5% or less. However, after complex febrile seizures, the risk of developing epilepsy is 10% to 20%.[109] Febrile seizures are not associated with sudden unexpected death in epilepsy.[109] [110] Epidemiologic data indicate that the vast majority of children with febrile seizures have a normal long-term outcome.[6] [111]

Genetic studies suggest that the relationship between febrile seizures and subsequent epilepsy and neurocognitive dysfunction is sometimes genetic, but there are complex interactions between genetic and environmental modifiers.[112]

Hippocampal abnormalities (mesial temporal sclerosis) and focal epilepsy are sometimes associated with prolonged febrile seizures.[69] Magnetic resonance imaging-detected brain abnormalities have also been reported in children following simple febrile seizures, and in adults with a history of simple febrile seizures in childhood.[113] [114] Therefore, febrile seizures may be less benign than generally thought.

The literature appears to support a role for febrile status in the development of focal epilepsy, but febrile status is clearly neither necessary nor sufficient on its own in the focal epileptogenesis process. Multiple insults are likely necessary for a child with febrile status epilepticus to develop epilepsy later in life.[115]

One study has shown that children who have febrile seizures are at a higher risk of developing psychiatric disorders in later life.[116]

Diagnostic guidelines

International

ACR appropriateness criteria: seizures - child (http://www.acr.org/Quality-Safety/Appropriateness-Criteria) [80]

Published by: American College of Radiology

Last published: 2020

Last published: 2015

Summary of recommendations for the management of infantile seizures: task force report for the ILAE Commission of Pediatrics (https://www.ilae.org/ guidelines/guidelines-and-reports) [81]

Published by: International League Against Epilepsy

Febrile seizures: guideline for the neurodiagnostic evaluation of the child with a simple febrile seizure (http://pediatrics.aappublications.org/ content/127/2/389) [1]

Published by: American Academy of Pediatrics Last published: 2011

Treatment guidelines

International

Febrile seizures: clinical practice guideline for the long-term management of the child with simple febrile seizures (http://pediatrics.aappublications.org/content/121/6/1281) [2]

Published by: American Academy of Pediatrics Last published: 2008

Treatment of pediatric epilepsy: expert opinion (https://www.ncbi.nlm.nih.gov/pubmed/16615562) [98]

Published by: Le Bonheur Comprehensive Epilepsy Program, University **Last published:** 2005 of Tennessee

Treatment of the child with a first unprovoked seizure (https://www.aan.com/Guidelines/Home/ByTopic?topicId=14) [105]

Published by: American Academy of Neurology; Child Neurology
Society

Last published: 2003 (reaffirmed 2021)

Summary of recommendations for the management of infantile seizures: task force report for the ILAE Commission of Pediatrics (https://www.ilae.org/guidelines/guidelines-and-reports) [81]

Published by: International League Against Epilepsy Last published: 2015

Treatment of pediatric epilepsy: European expert opinion (http://www.jle.com/fr/revues/epd/sommaire.phtml?cle_parution=2091) [106]

Published by: Le Bonheur Comprehensive Epilepsy Program, University **Last published:** 2007 of Tennessee; University Hospital Robert-Debré, Paris; Institute for Children and Adolescents with Epilepsy, Lyon

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Images

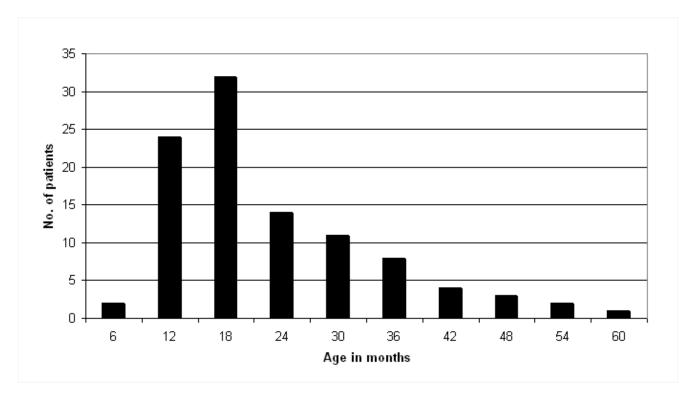


Figure 1: Age of occurrence of febrile seizures in 100 consecutive children treated in a university-affiliated tertiary care hospital: maximum frequency between ages 12 and 18 months, with a rapid decline after 24 months of age

Graph created by John J. Millichap, MD; used with permission

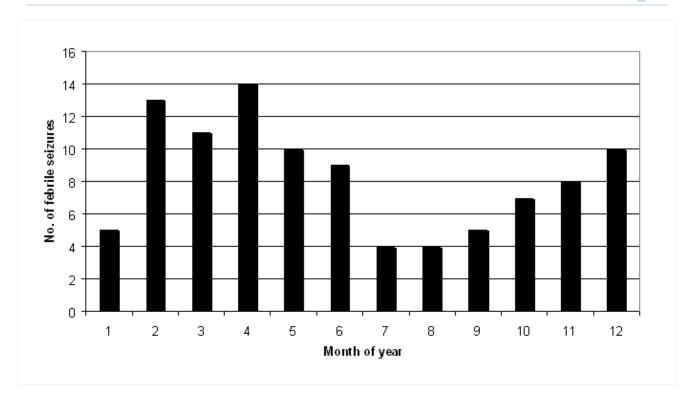


Figure 2: Seasonal occurrence of febrile seizures in 100 consecutive children treated in a university-affiliated tertiary care hospital: maximum frequency in spring and winter; lowest frequency in summer months

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Figure 1 – BMJ Best Practice Numeral Style

5-digit numerals: 10,000

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DISCLOSURES: DR declares that he is a previous member of the National Institute for Health and Care Excellence Feverish Illness in Children Guideline Group.

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Department of Neurology, University of Virginia Health System, Charlottesville, VA DISCLOSURES: RSR declares that he has no competing interests.