**Febrile Seizures**

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# Febrile Seizures

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**IMPORTANT POINTS**

1. **Most children who have febrile seizures do very well, and the risk of epilepsy is low.**
2. **The earlier the age at which the first febrile convulsion occurs, the more likely are recurrences.**
3. **Diagnostic laboratory tests never should be routine. Neuroimaging rarely is indicated.**
4. **Meningitis always should be ruled out, either clinically or by lumbar puncture if indicated.**
5. **Treatment has not been shown to reduce the risk of later epilepsy and carries a risk of side effects.**

## Definition

Febrile seizures are the most common convulsive disorder in young children. As defined in a 1980 National Institutes of Health consensus conference, a febrile seizure is:

> "An event in infancy or early childhood, usually occurring between three months and five years of age, associated with fever but without evidence of intracranial infection or defined cause. Seizures with fever in children who have suffered a previous nonfebrile seizure are excluded. Febrile seizures are to be distinguished from epilepsy, which is characterized by recurrent nonfebrile seizures."

This definition excludes seizures that accompany neurologic illnesses, such as meningitis, encephalitis, or toxic encephalopathy. Seizures in these instances do not carry the same prognosis as febrile seizures because the underlying illness may affect the central nervous system.

Febrile seizures have been discussed in the medical literature since the time of Hippocrates, but it was not until the middle of the present century that they were recognized as a separate syndrome distinct from epilepsy. An early classification proposed by Livingston divided them into "simple febrile seizures" and "epilepsy triggered by fever." He included in the latter definition febrile seizures that were prolonged or focal or that occurred in a child who has a family history of epilepsy. These definitions no longer are used because it has become clear through prospective epidemiologic studies that there is not nearly as great a risk for development of epilepsy or recurrent afebrile seizures as had been attributed by Livingston to the seizures he called "epilepsy triggered by fever".

More recently, febrile seizures have been divided into two subgroups: simple febrile seizures, which last fewer than 15 minutes and are generalized, and complex febrile seizures, which are prolonged, multiple within 24 hours, or focal. Children in either of these subgroups may have a pre-existing neurologic abnormality or a family history of febrile or afebrile seizures.

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## Epidemiology

Febrile seizures occur in approximately 2% to 4% of young children in the United States, South America, and Western Europe. They are reported to be even more common in Asian countries. Several large prospective studies have determined that in approximately 20% of cases, the first febrile seizure was complex (ie, lasted more than 15 minutes, was focal, or involved at least two seizures within 24 hours). The most common age of onset is in the second year of life. Febrile seizures are slightly more common in males.

### RISK FACTORS FOR A FIRST FEBRILE SEIZURE

In studies comparing children who have febrile seizures with febrile controls, a higher temperature was a risk factor for the development of a febrile seizure, as was a history of febrile seizures in a close relative. In a similar study in which both febrile and afebrile control children were examined, a family history of febrile seizures, neonatal discharge 28 days or later, parental report of slow development, and child care attendance were risk factors for febrile seizures (Table 1). Another recent study found a correlation between low serum sodium levels and risk for developing febrile convulsions.

### RECURRENCE

After the first febrile seizure, approximately 33% of children will experience one or more recurrences, and about 9% of children who have febrile seizures will have three or more. The younger the child when the first febrile seizure occurs, the greater the likelihood of recurrence. Most recurrences (75%) happen within 1 year. A recent study has shown an increased risk of recurrence to be associated with a shorter duration of fever before the initial febrile seizure and a lower temperature. Family history of febrile seizures is another reported risk factor for recurrence. A family history of afebrile seizures has been reported as a risk factor for recurrence in some studies, but not in others. "Complex" febrile convulsions are not more likely to be followed by recurrences. Young age of onset and a family history of febrile convulsions are the strongest and most consistent predictors of recurrence (Table 2).

### EPILEPSY

Although it has been reported that febrile seizures preceded 15% of

**TABLE 1. Risk Factors for a First Febrile Seizure**

| |
|---|
| • Family history of febrile seizures |
| • Neonatal discharge ≥28 days |
| • Delayed development |
| • Child care attendance |
| • Low serum sodium |
| • Very high fever |

**TABLE 2. Risk Factors for Recurrence of Febrile Seizure**

| |
|---|
| • Young age |
| • Family history of febrile seizures |
| • Short duration of fever before the initial seizure |
| • Relatively lower fever at the time of the initial seizure |
| • Possible family history of afebrile seizure |

cases of childhood onset epilepsy, because febrile seizures are a much more common occurrence than childhood epilepsy, fewer than 5% of children who have febrile seizures actually develop epilepsy.

Rates of epilepsy tend to be higher in populations having febrile seizures from selected sources such as hospital admissions or referrals to specialists. All types of epilepsy, including absence, generalized tonic-clonic, and complex partial, can be seen in patients who have a history of febrile convulsions.

In the National Institute of Neurologic Disorders and Stroke (NINDS) Perinatal Collaborative Project (NCPP), an increased risk for developing one or more afebrile seizures was found among children in whom development was suspect or abnormal prior to the first febrile seizure, whose parent(s) or sibling(s) had a history of afebrile seizures, and who had a complex first febrile seizure (Table 3). Of the 60% of children who had febrile seizures in the NCPP and none of these risk factors, 2% developed at least one afebrile seizure by age 7 years. Of the 34% who had one risk factor, 3% developed one or more afebrile seizures, and if two or more risk factors were present, the afebrile seizure rate increased to 13%. A prior neurologic abnormality identified by examination also was associated with an increased risk for later afebrile seizures, but there was no increased risk from having had multiple episodes of febrile seizures.

**TABLE 3. Risk Factors for the Development of Epilepsy Following Febrile Seizures**

| |
|---|
| • Suspect or abnormal development before the first seizure |
| • Family history of afebrile seizures |
| • Complex first febrile seizure |

#### GENETICS

Febrile seizures tend to occur in families, although the exact mode of inheritance is not known. Children who have febrile seizures tend more often to have a history of febrile convulsions in close relatives. There also may be a higher incidence of afebrile seizures in the families of children who have febrile seizures, but the evidence is not as clear. The relative risk for epilepsy is higher in siblings of children who have febrile seizures, but not in other relatives.

Parents may ask about the risk of febrile seizures in younger siblings of children who have febrile convulsions. It is in the range of 10% to 20%, but will be higher if the parents have a history of febrile convulsions.

#### COMPLEX PARTIAL SEIZURES

Although some authors believe that febrile seizures may predispose the child to developing complex partial seizures (CPS), the evidence is controversial. Studies of patients who have CPS and a history of prolonged febrile convulsions in early childhood show an increase in mesial temporal sclerosis. Although there may be an association between febrile convulsions that are prolonged or focal and later CPS, a causal relationship has not been proven. Only a very small percentage of children who have febrile seizures develop CPS, and it may be that the child who is neurologically at risk is more likely to have both febrile and complex partial seizures.

## Pathophysiology: Etiology

Most febrile illnesses associated with febrile seizures are due to common infections such as tonsillitis, upper respiratory infections, and otitis media. Children of preschool age are subject to frequent infections and accompanying high fevers, which in combination with a relatively low seizure threshold, allows for the common occurrence of febrile seizures.

Several recent reports have documented the frequent presence of human herpesvirus 6 (HHSV-6) in cases of febrile seizures. HHSV-6 is a recently identified etiologic agent in roseola (exanthem subitum). In one series, the virus was cultured from 8 (19%) of 42 patients who had a first febrile seizure, and titers rose in 9 of the 34 (26%) who returned for convalescent titers. The virus was not detected in 29 cerebrospinal fluid (CSF) samples taken. In eight patients who had a history of roseola and multiple febrile convulsions, HHV-6 DNA was detected in the CSF sampled after a febrile convulsion; it was not evident in controls, and it was documented in only one of seven children who had a single febrile seizure. It was postulated that viral invasion of the brain may occur sometime during the acute illness, and during subsequent illnesses, be reactivated by fever.

## Clinical Aspects

Febrile seizures usually occur early in the course of a febrile illness, often as the first sign. It commonly has been thought that the rate of increase of the fever is an important trigger, but there are no data to support the importance of this factor over the height of the fever. The seizure may be of any type, but the most common is tonic-clonic. Initially there may be a cry, followed by loss of consciousness and muscular rigidity. During this tonic phase, there may be apnea and incontinence. This is followed by the clonic phase of repetitive, rhythmic jerking movements and then by post- ictal lethargy or sleep.

Other seizure types may occur, such as staring with stiffness or limpness, jerking movements without prior stiffening, or only focal stiffness or jerking. Most seizures last fewer than 6 minutes; fewer than 8% last longer than 15 minutes. Thus, the child who has a febrile seizure usually is not brought to medical attention until after the seizure has ended.

When a child is seen following a febrile convulsion, it is important to identify whether there is an underlying illness requiring treatment. A history should include inquiries as to symptoms of infectious illness, medication exposure, trauma, developmental level, and family history of febrile or afebrile seizures. A complete description of the seizure should be obtained from an eyewitness. In the physical examination, the level of consciousness, the presence of meningismus or a tense or bulging fontanelle or of Kernig or Brudzinski sign, and any abnormalities or focal differences in muscle strength or tone should be noted carefully and reassessed periodically.

Other causes of seizures associated with fever must be ruled out, especially encephalitis or meningitis. A lumbar puncture (LP) is indicated if there is any clinical suspicion of meningitis. The presence of a source of infection such as otitis media does not rule out meningitis, and if the infant has been taking antibiotics, partially treated meningitis should be suspected and an LP performed.

Typical clinical signs of meningitis may be absent in those younger than 12 to 18 months of age. In general, the threshold for performing an LP should be low, and it should not be omitted on the sole basis of age, family history, or previous number of febrile seizures. If increased intracranial pressure is suspected, the decision to perform an LP must be made by an experienced physician who will weigh the risk of delaying a diagnosis of meningitis against the risk of an LP.

Other causes of seizures associated with fever other than meningitis or encephalitis include infections such as roseola infantum and *Shigella* gastroenteritis; certain toxins or drug exposures, including diphenhydramine, tricyclic antidepressants, amphetamines, and cocaine; and dehydration causing electrolyte imbalances.

Routine laboratory studies are not indicated and should be performed only as part of the evaluation for a source of fever. Skull radiographs and neuroimaging such as computed tomography (CT) or magnetic resonance imaging (MRI) are seldom helpful and should not be performed routinely. The electroencephalogram (EEG) has not been shown to be helpful in the evaluation of febrile seizures. An EEG obtained up to 1 week after a febrile seizure may show an abnormality, usually consisting of occipital slowing. Although there is a higher incidence of EEG abnormalities in children who have febrile seizures, which increases with age, the EEG does not help predict recurrences or risk for later epilepsy.

## HOSPITALIZATION

The decision to admit the child who has experienced a febrile seizure for overnight observation in the hospital depends on the specific clinical situation and the family circumstances. The child should be kept in the emergency department holding area or doctor's office for at least several hours and re-evaluated. Most children will have improved and be alert, and if the cause of the fever has been diagnosed and treated appropriately, they may be sent home. However, follow-up care must be assured. If the child's clinical situation remains unstable, if there is any question of possible meningitis, or if parents seem unreliable or unable to cope, hospitalization is advisable. About 16% of children may experience another seizure within 24 hours, but it is not known how to predict in which cases seizures may recur immediately.

## PARENTAL COUNSELING

Febrile seizures are very frightening events, and it is not uncommon for parents to state that they believed that their child was dying during the seizure. They first must be reassured and then given instructions on the management of possible recurrences. Information and counseling should be provided after the acute event and at a later time, when parents have had a chance to formulate questions.

A written handout is usually helpful. The following points should be stressed:

1. Although febrile seizures are frightening, they do not cause brain damage, and the likelihood of developing epilepsy or recurrent nonfebrile seizures is very small.
2. There is, however, a risk of further febrile seizures during the current or subsequent febrile illnesses.
3. If another seizure occurs, stay calm, place the child on his or her side or abdomen with the face downward; do not force anything between the teeth and observe the child carefully. If the seizure does not stop after 10 minutes, the child should be brought to the nearest medical facility by car or ambulance.

***Routine laboratory studies are not indicated (for patients who have febrile seizures) and should be performed only as part of the evaluation for a source of fever.***

Vigorous control of fever by antipyretics and sponging often is advocated but has not been proven to lower the risk of febrile seizures recurring. Often, seizures occur as the first sign of a febrile illness. Lowering fevers by appropriate use of antipyretics such as acetaminophen usually will make the child more comfortable. However, some authors have suggested that antipyretics may prolong viral shedding and impair the body's ability to respond to viral infection.

Questions often arise regarding continuation of routine childhood immunizations. Studies have indicated that seizures following childhood immunizations are no different from other febrile seizures. Seizures may occur most commonly following a pertussis or DPT immunization because the pertussis component commonly provokes a fever. In each child, the advantages conferred by vaccines must be weighed against the risk, and if immunization is postponed, the situation must be re-evaluated at each subsequent visit. The period of greatest risk for febrile seizure recurrences is up to 48 hours following a DPT immu-

nization and 7 to 10 days after a measles immunization.

### LONG-TERM MANAGEMENT

The approach to long-term management should focus on decreasing parental anxiety. Whether prophylaxis with medication is effective is controversial. Side effects occur, and antipyretics alone have not been shown to be effective in preventing febrile seizure recurrences. There is no evidence that the treatment to prevent recurrences can prevent the subsequent development of epilepsy.

Diazepam and phenobarbital have been used to prevent recurrences of febrile seizures, although not all studies have confirmed their efficacy. Prescription of prophylaxis should be reserved only for the rare cases in which multiple seizures have occurred in a child who still is very young, there has been focal paralysis following a seizure, or the parents' anxiety level remains very high even after reassurance.

Diazepam has been administered orally and rectally to prevent recurrences only during a febrile illness. Phenobarbital 5 mg/kg per day has been given continuously in a daily or twice-daily dosage. There are significant drawbacks to both treatments; diazepam may cause ataxia and lethargy, and phenobarbital may cause behavior problems and affect intellectual performance adversely.

If treatment is prescribed, oral diazepam is preferable and may be given in three divided doses to total 1 mg/kg per day when the child is ill or feverish. If side effects of lethargy or ataxia occur, the dosage should be halved, and the physician must evaluate whether the lethargy could be masking an underlying illness such as meningitis. Diazepam in both oral and rectal forms has been used successfully in countries outside of the United States.

## Conclusion and Prognosis

Febrile seizures now are recognized as a benign syndrome determined largely by genetic factors, manifested by an age-related susceptibility to seizures that eventually is outgrown. Although febrile seizures are extremely frightening to parents, children almost always do quite well. Only a small minority will develop epilepsy or recurrent nonfebrile seizures later. Unless seizures are exceedingly long, there is no evidence of risk of brain damage, and large studies have documented the lack of later intellectual and motor handicap as a result of febrile seizures.

Long-term management of febrile seizures should focus on decreasing parental anxiety. Treatment to prevent recurrences has not been shown to prevent the later development of epilepsy. Treatment to prevent recurrences should be recommended in only a small minority of children who have febrile seizures. Potential risks of anticonvulsant therapy should be weighed against benefits. No currently available treatment has been shown to be both completely safe and effective. Fortunately, the majority of children who have febrile seizures will require no treatment other than parental reassurance and will have a good outcome.

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## PIR QUIZ

1. Which one of the following statements about recurrence of febrile seizures is *true*?
   A. A complex first febrile seizure is more likely to recur than a simple febrile seizure.
   B. A first febrile seizure occurring at 6 months of age is more likely to recur than one occurring at 3 years of age.
   C. A first febrile seizure with fever of 104˚F (40˚C) is more likely to recur than one with fever of 101˚F (38.3˚C).
   D. Girls are more likely than boys to have recurrence of febrile seizures.
   E. Longer duration of fever before the initial febrile seizure is a risk factor for recurrence compared with shorter duration of fever.

2. Which one of the following is the *most* important risk factor for developing epilepsy following febrile seizures?
   A. A complex first febrile seizure.
   B. A history of febrile seizures in the family.
   C. Female gender.
   D. Multiple episodes of febrile seizures.
   E. Younger age of onset of first febrile seizure.

3. A 6-month-old child who has a history of fever of 2 days' duration presents with generalized tonic-clonic seizures lasting approximately 10 minutes. Physical examination reveals a rectal temperature of 103˚F (39.4˚C), slightly bulging fontanelle, bilateral otitis media, and lethargy. The infant is arousable but irritable. Which one of the following is the *most* appropriate initial diagnostic test?
   A. Computed tomographic scan of the head.
   B. Electroencephalography.
   C. Lumbar puncture.
   D. Magnetic resonance imaging of the brain.
   E. Serum electrolyte levels.

4. Which one of the following statements about the management of a child who has had a febrile seizure is *true*?
   A. Continuous phenobarbital prophylaxis will prevent development of epilepsy in subsequent years.
   B. Immunization with diphtheria-pertussis-tetanus (DPT) should be carried out using half the standard dose.
   C. Management should be guided by serial electroencephalographic studies.
   D. Parents should be reassured of the benign nature of febrile seizures and given instructions for handling a possible recurrence.
   E. Use of antipyretics at the first sign of fever has been shown to decrease the recurrence of febrile seizures.

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