By Nishi Rampal, MD and Steven Karceski, MD

Hot Topic: How to Respond to Febrile Seizures

Does this event necessarily lead to development of epilepsy? Here's how to assess the risk, and minimize it.

Febrile seizures can be extremely frightening to parents and caregivers, typically prompting an urgent health care visit. One in 25 children in the US have a single febrile convulsion. One-third or more (about 40 percent)[1] of these children will suffer subsequent febrile seizures.[2] It is one of the most common neurologic issues of childhood, and the most common convulsive event, according to the International League Against Epilepsy. Fortunately, the majority of febrile seizures are benign.

For many parents, reassurance that the seizure does not signify a more serious problem is all that is needed. At the same time, however, febrile seizures are a risk factor for the later development of epilepsy. Approximately two to four percent of children who have a febrile seizure will later develop recurrent unprovoked seizures.[1] There are two types of febrile seizures: *simple* or *complex*. As we will discuss, accurate counseling, prognosis and management of febrile convulsions depends on the type of seizure that occurs.

What is a Febrile Seizure?

It's a seizure that occurs in childhood between one month and five years of age, with a peak at 18 to 22 months. By definition, it is associated with a febrile illness. The seizure risk is associated most strongly with the rate of rise rather than the absolute temperature of the fever. In most cases, the temperature will exceed 101°F. By definition, the febrile seizure *cannot* be caused by infection of the central nervous system (*e.g.,* meningitis).

Febrile seizures are associated with any type of common childhood infection. The infection can be bacterial or viral (often seen in human herpesvirus-6, also called roseola or sixth disease) and can be seen in fevers that accompany vaccinations such as the measles–mumps-rubella (MMR) vaccine. Children who experience febrile seizures are at an age when infections are common, such as upper respiratory infections, otitis media and gastrointestinal illnesses. There is a slight preponderance of febrile seizures in children who are enrolled in daycare, likely reflecting their exposure to a variety of common infectious agents.

A family history of febrile seizures is a risk factor: the occurrence of febrile seizures may be due to a genetically inherited lower seizure threshold. Current evidence suggests that if a child has a febrile seizure, their sibling has a 10 to 15 percent chance of having one as well. If their parent had a febrile seizure, that risk can go to as high as 60 percent. Genetic studies have identified at least seven genetic loci that seem to be associated with the inheritance of febrile seizures. The inheritance patterns appear to be autosomal dominant, with variable penetrance of phenotypes (ranging from 30 to 70 percent). Studies have not shown a predilection for a particular race or gender, however there might be an increased incidence in males.

Simple vs. Complex Febrile Seizures

Simple febrile seizures account for about 75 percent of all febrile seizures and have three features. They are generalized tonic-clonic seizures. In other words, there are no focal neurological signs during the seizure itself, such as forced head deviation or unilateral dystonic posturing of the extremities. Studies have shown that 78 percent of simple febrile seizures last less than three minutes (Hesdorffer, personal communication). Twenty-two percent lasted more than 20 minutes. The "cut-off" for the duration of a simple febrile seizure has therefore been set at less than 15 minutes. Finally, simple febrile seizures should not recur in less than 24 hours.

Conversely, a febrile seizure is deemed complex if even a single parameter strays (see Table 1). A seizure with focal neurological features, a convulsion that lasts more than 15 minutes, or two or more convulsions within 24 hours is classified as a complex febrile seizure. Complex events account for about 25 percent of all febrile seizures. The National Collaborative Perinatal Project studied 55,000 infants, with 1706 first febrile seizure events. Twenty-eight percent of the initial febrile seizures were complex: four percent focal, eight percent prolonged >15 minutes, and 16 percent with recurrence within 24 hours. A Todd's paresis occurred in 0.4 percent.[3]

Febrile Seizures and Epilepsy

There is a difference between febrile seizures and epilepsy. Although the former can occur more than once, because they are provoked, their occurrence does not constitute epilepsy. In contrast, epilepsy is the syndrome of recurrent unprovoked seizures. This becomes a little confusing as febrile seizure are a risk factor for the later development of epilepsy.

Table 1. Simple Versus Complex Febrile Seizures

Simple Febrile Seizure	Complex Febrile Seizure
Generalized seizure (convulsion)	Focal features are present
Less than 15 minutes	More than 15 minutes
1 seizure in a 24 hour period	More than 1 seizure in a 24-hour period

Table 2. Seizure First Aid

For febrile seizures lasting less than five minutes:

- If the person is falling, help him or her to the ground. Protect the person from nearby hazards.
- Loosen any tight or restrictive clothing.
- Turn the person on their side in order to keep the air passages open.
- Reassure the person as they awaken from the seizure.
- **Do not** place anything in the person's mouth. A person who has a seizure cannot swallow their tongue. However, objects which are placed in the mouth can cause injury or choking.
- **Do not** restrain the patient.
- **Do not** panic. Most febrile seizures stop on their own after one to three minutes.

More specifically, febrile seizures are a risk for the development of mesial temporal sclerosis (1 in 75,000), a cause of temporal lobe epilepsy.

Febrile seizures are a risk factor for (1) more febrile seizures and (2) the later development of epilepsy. After the first febrile seizure, the risk of subsequent febrile seizures is about 30 to 40 percent.[1] After the second event, the risk of recurrence climbs to about 60 percent. Factors that increase likelihood of recurrence include: initial complex febrile seizure, onset of first febrile event prior to one year of life (50 percent recurrence rate), temperature <104°F/<40°C at seizure onset, a short interval between febrile seizures, and a family history of febrile seizures. The incidence of developing epilepsy following a simple febrile seizure is two to four percent. Following a complex febrile seizure, the incidence of developing epilepsy is five to 10 percent.

Risk for a first febrile convulsion climbs to 30 percent in selected populations compared to age-matched controls at four percent[4] if two or more of the following independent risk factors are present: (1) a first or second degree relative with febrile seizures, (2) delayed neonatal discharge of greater than 28 days of age, (3) parental report of slow development, and (4) day care attendance. Offering anticipatory guidance to families at high risk can be considered.

Evaluation and Management

As with many seizure disorders, the correct diagnosis depends on a careful history and patient examination. Medical testing, such as routine serum tests should be guided by the clinical scenario and are not routinely necessary. However, careful consideration for a primary CNS infection or meningitis is included in the practice parameters of both the American Academy of Neurology and American Academy of Pediatrics. Children below the age of 18 months deserve a very careful evaluation, as meningeal signs may be absent or subtle, often necessitating a lumbar puncture to complete the evaluation.

Imaging including CT and MRI should be reserved for complex febrile seizures. In other words, neuroimaging should be performed if the seizure has focal features, if multiple seizures occur in less than 24 hours, or if it is prolonged (more than 15 minutes). Additionally, if the clinician suspects a structural lesion, if there is a history of developmental delay, abnormal head circumference, focal neurological findings, or neurocutaneous lesions, neuroimaging is needed.

Electroencephalography (EEG) is routinely ordered in the evaluation of seizures. It is often requested in the setting of a febrile seizure. However, whether performed immediately following the event or over the next 30 days, EEG does not predict the risk of a recurrent febrile seizure or epilepsy. This is true both for simple febrile and complex febrile events.4 In other words, in this situation, EEG is not usually helpful.

Prognosis

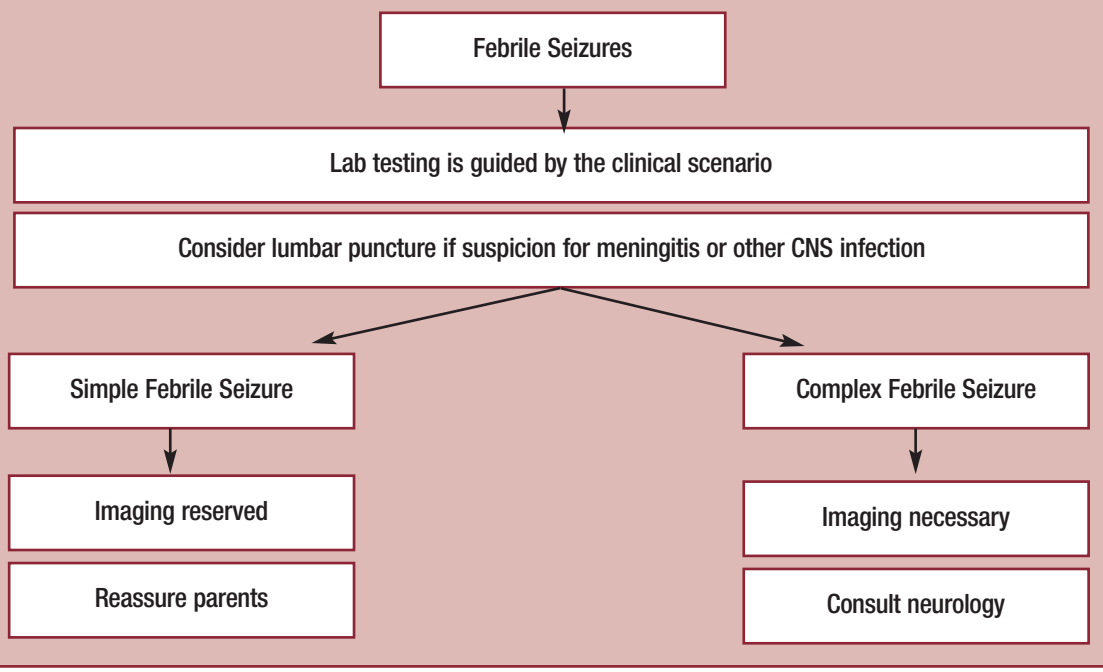
Multiple studies including The National Collaborative Perinatal Project study showed no evidence that febrile convulsions damage the brain, even in 27 patients with febrile seizures lasting >30 minutes.[1] One in 75,000 children who have had febrile seizure(s) will later develop temporal lobe epilepsy. In these cases, the cause is mesial temporal sclerosis. When it occurs, it is refractory, that is, resistant to medications, in up to 89 percent. As already discussed, approximately one- third of febrile seizures recur. The risk for developing epilepsy ranges from two percent after a simple febrile seizure, and fove to 10 percent after a complex febrile seizure.

Treatment

When a seizure occurs, the patient should be placed on his or her side and observed closely. In other words, seizure first aid should be followed (see Table 2). All patients who experience their first febrile seizure should be evaluated by a

By Nishi Rampal, MD and Steven Karceski, MD

Table 3. Management of Febrile Seizures



physician urgently, whether by a primary physician or an emergency room specialist. Events that last greater then 15 minutes should be emergently evaluated, as these are by definition complex (see Table 3).

It seems logical to treat the fever, thereby preventing the febrile seizure. However, multiple studies have shown that administration of antipyretics do not prevent the febrile seizure.[1,6-8] Reflecting this, the International League Against Epilepsy does not recommend antipyretic use other than for patient comfort.

There are rare cases where seizure-specific treatments may be considered. For instance, there is a small subset of children who have simple febrile seizures often, perhaps with every febrile illness. Although there is no universal agreement on this point, some physicians argue that anti-seizure treatment is needed in these cases. Their point is simple: medications have been shown to reduce the frequency of simple febrile seizures. Phenobarbital and Diazepam are two of these agents.[9] Valproate, while effective, carries several risks in this age group including fulminant hepatitis and pancreatitis and thus should be avoided.

Parents with a child at risk of having febrile seizures are often instructed on home management. The most important consideration is to ensure the safety of the child by removing any chance of injury during the convulsion. While keeping an eye on the length of the seizure, parents can be taught to administer a single dose of rectal diazepam gel at a dose of 0.5mg/kg. The decision to use rescue therapy for prolonged febrile seizures must be made on a case-by-case basis, guided by the clinical situation.

Conclusions

Febrile seizures most often occur in children between the ages of six to 22 months. Events should be classified as simple or complex, and evaluated as such. While most febrile seizures are benign, there is a small risk of developing epilepsy later in life. In most instances, seizure first aid and reassurance of parents is all that is required. However, in a small subset of children, antiseizure medication may be needed to either reduce seizure frequency or decrease the duration of the event(s). **PN**

1. Camfield PR, CS Camfield, and DG Hirtz. Treatment of Febrile Seizures. IN: Epilepsy: A Comprehensive Textbook, edited by J. Engle, JR., and T.A. Pedley. Lippincott-Raven Publishers, Philadelphia, 1997. Pp. 1305-1309.

2. Nelson KB and Ellenberg JH. Predictors of epilepsy in children who have experienced febrile seizures. N Engl J Med 1976;295(19):1029-1033.

3. Nelson KB and Ellenberg JH. Prognosis in children with febrile seizures. Pediatrics 1978;61:720-777.

4. Bethune P, Gordon KG, Dooley JM, Camfield CS, Camfield PR. Which child will have a febrile seizure? Am J Dis Child 1993;147:35-39.

5. Kuturec M, Emoto SE, Sofijanov N. et al. Febrile seizures: is the EEG a useful predictor of recurrences? Clin.Pediatr.(Philadelphia). 1997;36:31-6.

6. Rutter N, Metcalfe DH. Febrile convulsions – what do parents do? Brit Med J 1978;2(6148):1345-1346.

7. Uhari M, Rantala H, Vinionpaa, Kurttila BM. Effect of acetaminophen and of low dose intermittent diazepam on prevention of recurrent febrile seizures. J Pediatr 1995;126:991-995.

8. Van Stuijvenberg M, Derksen-Lubsen G, Steyerberg EW, Habbema JD, Moll HA. Randomized, controlled trial of ibuprofen syrup administered during febrile illnesses to prevent febrile seizure recurrence. Pediatrics 1998;152:1170-1175.

9. Pust B. [Febrile seizures--an update]. Kinderkrankenschwester. 2004;23:328-31.

Nishi Rampal, MD is a Fellow in Critical Care and Epilepsy at Columbia University, after completing neurology residency at Yale University.

Steven Karceski, MD is Assistant Clinical Professor of Neurology at the College of Physicians & Surgeons of Columbia University and Director of the Columbia Epilepsy Center at the Atlantic Neuroscience Institute.