

FEBRILE SEIZURES: AN UPDATE

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Febrile seizures (FS) are the most common seizures in children. Controversy continues to exist with regard to the precise definition, diagnostic evaluation and especially the treatment. The objective of this update is to highlight the current recommendations for the approach and management of this distressing disorder in the light of recent trends.

Definition

The most widely accepted definition is the one by the NIH Consensus Panel (USA, 1980) which defines febrile convulsion as an event in infancy or childhood usually occurring between 3 months and 5 years of age, associated with fever, but without evidence of intracranial infection or defined cause. Seizures with fever in children who

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have suffered a previous nonfebrile seizure are excluded. Febrile seizures are to be distinguished from epilepsy which is characterized by recurrent nonfebrile seizures(1). A rectal temperature of 38° C or more is usually accepted in this definition.

It should be borne in mind that all seizures with fever are not benign febrile seizures. "Febrile convulsions" should be distinguished from "convulsions with fever" which include any seizure in a child of any age with fever of any cause like those with pyogenic meningitis, hypernatremic dehydration or other metabolic diseases. These may carry a more ominous prognosis than that of febrile seizures owing to the effects of associated illness.

Children with pre-existing neurodevelopmental abnormalities may also have FS, and such children are included in the definition of the Consensus panel(1). However, there is some difference of opinion on this because the prognosis in these children is determined by the degree and type of the underlying abnormality(2). The Joint Working Group of British Physicians and Pediatricians have, therefore, limited their definition of FS to include only 'neurologically normal children'(3). This controversy cannot be resolved here. In our practice, we identify such children with FS separately for purpose of follow up and prognosis.

Epidemiology

Febrile seizures occur in 3-4% of children under the age of 5 years(4).

Usually these do not occur beyond the age of 5 years implying a specific vulnerability of young children to fever as a precipitant. The median age of occurrence is 18-22 months(5).

There is a genetic predisposition to febrile seizures. The risk of another child having FS is one in five after one affected child, and one in three if both parents and a previous child have had febrile seizures(6).

Classification

Commonly febrile convulsions are classified into simple (benign/typical) and complex (atypical). Simple seizures constitute about 85% of febrile seizures. These are generalized, last less than 15 minutes, and do not recur during the same illness.

Complex febrile seizures constitute about 15% of FS and are associated with one or more of the following: (i) Focal features, (ii) Duration more than 15 min, and (iii) Multiple, *i.e.*, more than one seizure within 24 hours. The classification is helpful for determining the risk of recurrence and epilepsy.

Risk of Recurrence

This is depicted in *Table 1*(7). The overall recurrence rate is only 25-30%. Most recurrences (75%) occur within one year of the first febrile seizure. The risk of recurrence is in fact highest during the first few months after the seizures, and rapidly declines after several months without seizures.

A number of studies have found various factors to be associated with increased risk of recurrence of febrile seizures(4,8-12). A meta-analysis(13) of

TABLE I—Risk of Recurrence after Febrile Seizures

Risk of another febrile seizure	
After 1 seizure	30%
After 2 seizures	40%
After 3 seizures	40%
3 or more recurrences seen in 4-9% cases	

Adapted with permission from Freeman *et al.*(7).

14 such studies done upto 1986 has found only 2 such consistent associations: (i) younger age of onset, and (ii) family history of febrile seizures. Subsequently, two more factors have been added—(i) lower temperature at the time of FS(14), and (ii) shorter duration of temperature before the FS(15).

Age of onset is perhaps the single strongest and most consistent predictor of recurrent febrile seizures the younger the child the greater the risk (50% in <1 year old versus 20% in >3 years old)(5). However, a recent study has found the highest hazard of recurrence between 12-24 months of age(16).

The higher recurrence risk associated with early age at onset may indicate increased vulnerability to febrile seizures or may simply be a function of the greater remaining risk period available in which to have a recurrence. It has been shown that the recurrence risk is a function of attained age, not age at first febrile seizure(10), and that the child's age at each subsequent seizure has predictive value for further seizures—the younger the child at the second and third seizures, the higher the likelihood of further recurrences(16).

A family history of febrile seizures has been found to increase the risk of recurrence by approximately 20%(13). Family history of unprovoked seizures, on the other hand, does not appear to be as strong a risk factor for recurrence(13).

A lower temperature at the time of the first febrile seizure has a strong association with the recurrence risk(14) (66% with <40°C versus 10% with >40°C). A shorter duration of fever before the initial febrile seizure is also associated with an increased risk of recurrence(15).

Complex features have not been strongly or consistently associated with an increased risk of recurrence(13), even though some studies had documented such an association(9-11). Even febrile status epilepticus (seizures >30 minutes) has not been associated with an increased risk of recurrence(13).

The presence of pre-existing or subsequent neurological abnormality may increase the risk of recurrence(4,9,12,17), but the magnitude cannot be estimated(13).

It is now being recognized that none of the risk factors alone identify children at high or low risk of recurrent seizures(15,16). The risk is better predicted by a combination of risk factors which act in a cumulative way and can identify groups of various risk categories(9-11,13). With such subgrouping, most children (65-75%) fall into a low recurrence risk, of <30%, with only a minority (3-10%) having a high (>75%) risk, and the others intermediate (40-50%) recurrence risk(13).

Risk of Epilepsy

Population based studies have

shown that the overall risk of epilepsy after febrile convulsions is only 2-2.5%(4,18). The factors increasing the risk of subsequent epilepsy are (Table II): (i) Complex febrile seizures,—the three complex features of febrile seizures are independent predictors of later afebrile seizures(7,13,15); (ii) Family history of afebrile seizures; and (iii) Presence of neuro-developmental abnormality.

In neurologically normal children the number of febrile seizures is only weakly associated with the risk of later epilepsy(13).

Different types of seizures (including absence, complex-partial and generalized tonic clonic) may occur in those children who develop epilepsy after previous febrile seizures. Although it was earlier believed that febrile seizures are associated with an increased risk of partial complex seizures(12), recent

TABLE II- Risk of Epilepsy After Febrile Seizures

Overall risk after febrile seizures	2.0-2.5%
Risk of epilepsy after 1 febrile seizure	
0 risk factors	1.0%
1 risk factors	2.5%
3 risk factors	5-10.0%

Note: Risk factors: Seizures prolonged >15 minutes, onesided, or 2 or more seizures during the same day; parent or brother or sister with epilepsy; neurologic disorder or developmental delay.

Adapted with permission from Freeman *et al.*, (7).

studies have not documented such an association(4,18,19) and the controversy continues(20). Abnormalities seen on the EEG either acutely or in later follow up do not predict the later development of epilepsy(19).

Intellectual and Motor Function

There is no evidence that febrile seizures cause a decrease in intellectual function, or increase the risk of mental retardation, cerebral palsy, injury or death(21).

Treatment of Acute Attack

Most febrile seizures are brief and would be over by the time a child is brought to the doctor. If the child is still having a seizure, it needs to be managed just like any other seizure, with maintenance of a clear airway, a semiprone position to minimize the risk of aspiration, and monitoring of vital signs. The seizures can be terminated by intravenous diazepam or lorazepam. Rectal diazepam 0.5 mg/kg is safe and effective. It is completely absorbed, and plasma concentration is obtained within 5-10 min, almost as rapidly as when it is given into a vein(22). The undiluted intravenous preparation is sucked in a small syringe and given through a polythene tube which is gently inserted 4-5 cm into the anus, after lubricating with vaseline. This method has also been advocated for home based management of convulsions by the parents. They have to be taught the technique and informed about the exact dose needed for their child. They are advised to keep one dose available at home so as to give it soon after the onset of a convulsion, and not to give if the convulsion has stopped.

Although there is no evidence that reducing the temperature prevents recurrences of febrile seizures, yet treatment of fever is generally advised. Paracetamol is effective; physical methods like fanning, and sponging may be used if needed but they cause discomfort and are not therefore routinely recommended.

Hospitalization

There is controversy on whether a child with febrile seizures should be admitted to hospital. The main concern is about overlooking meningitis, especially in a child with the first febrile seizure. Whereas some are of the opinion that all children with a first febrile seizure should be admitted, others(3) have considered the following selection criteria for admission: (a) Complex features; (b) Age of child <18 months; (c) Early review by doctor at home not possible; and (d) Home circumstances inadequate, or more than usual parental anxiety, or parents' inability to cope. It must be remembered that a history of previous convulsions does not rule out the possibility of meningitis. Any child who is ill-looking or in whom there is a slightest suspicion of meningitis, must be admitted irrespective of the above criteria.

Investigations

The two main objectives of investigating a child with febrile seizures are to rule out meningitis and ascertain the cause of fever. Viruses are the most common cause of illnesses in children admitted to the hospital with a first febrile seizure(23). Infections are usually upper respiratory, otitis media, and gastrointestinal. Quite often the seizures

occur during the early phase of rising temperature, before the parents realize that the child is ill. It is unusual for febrile seizures to occur after the first day of a febrile illness and should make one consider other diagnostic possibilities[^]). Seizures occurring after immunizations are likely to be febrile, occurring in response to temperature elevation, especially those occurring within 48 hours of DPT and 7-10 days after measles immunization[^]). No investigations are routinely necessary in all children after a febrile seizure. The battery of investigations is generally determined by the suspected cause of febrile illness rather than by the seizure, with the possible exception of lumbar puncture(3).

Lumbar puncture need not be routinely performed. The indications are shown in *Table III*. Ideally this decision should be taken by an experienced pediatrician who may at times decide not to do a lumbar puncture even in an infant if the child is active and alert and if the cause of fever can be ascertained. However, the decision should be reviewed within a few hours. Whenever in doubt, the investigation should be performed. The spinal fluid findings may be normal in early meningitis, thus a negative

TABLE III -*Indications for Lumbar Puncture in Children with Febrile Seizures*

1.	Clinical signs of meningism
2.	Undue or unexplained drowsiness or irritability
3.	Signs and symptoms of systemic illness
4.	Infants too young to reliably show clinical signs of meningitis—especially below 1 year age.

spinal tap does not eliminate the need for careful follow up.

EEG

An EEG is not a guide to treatment or to prognosis, and as such it is not helpful in children with first or recurrent febrile seizures(3).

The EEG, if done soon after the seizure, usually shows marked generalized slowing which may persist up to a week or more and may be asymmetrical(5). Abnormalities seen after the post ictal period include spikes, 4-6/sec slow waves, or spike waves(24-26). Specific abnormalities are more commonly seen in older children, in those with multiple previous febrile seizures, preexisting motor abnormality, and after focal seizures(26). However, these abnormalities are neither predictive of subsequent epilepsy nor, (*k* recurrences. An EEG may occasionally be needed in cases where febrile seizures are followed by focal neurologic abnormalities, to help rule out underlying structural lesions. Even in these cases, neuroimaging is more useful.

Long Term Management

There is no evidence that the prophylactic use of anticonvulsants prevents the subsequent development of epilepsy(3,21). Prevention of recurrences thus remains the major plausible goal for long term prophylaxis of febrile seizures.

Continuous Prophylaxis

Phenobarbitone 4-5 mg/kg/day has been shown to decrease recurrences and may decrease the chance that a subsequent FS, if it occurs will be prolonged

or focal(27-29). The major disadvantages of its use are its frequent and substantial side effects especially on cognitive and behavioral functions. Sodium valproate 30-40 mg/kg/day is equally effective for prophylaxis(30,31). Although it is much less likely to cause behavioral side effects and sedation, it has been reported to cause gastrointestinal upset, pancreatitis, serious hepatotoxic effects and even deaths especially in infants and very young children. It is, therefore, not recommended as a first line drug for the prophylaxis of febrile seizures. The continuous oral administration of either phenytoin(32) or carbamazepine(33) is not effective in preventing febrile seizures.

Intermittent Prophylaxis

Phenobarbital used intermittently in usual doses is ineffective in preventing recurrences(27). Phenytoin and carbamazepine have never been used intermittently. There is some evidence that valproate may be effective when used at times of fever(34), but its use for prophylaxis is unconfirmed.

Diazepam, administered rectally as suppositories(31,35,36) or solution(11,37), or orally(38-40), intermittently, at the onset of fever has been shown to be effective in preventing recurrence. The solution has a quicker and better absorption than suppositories and is, therefore, useful not only prior to a seizure but also at imminent seizures and during seizures(22). The data on oral prophylaxis are promising but incomplete(22). By either route, generally a dose of 0.3-0.5 mg/kg (maximum 10 mg) is used and repeated every 8-12 hours(37) if the temperature is 38°C or

more. A maximum of 4-5 doses are given per illness. Other than short term sedation, ataxia and at times hyperexcitability, there are few significant side effects with such therapy(41).

The main problem envisaged with intermittent prophylaxis is that parents may not be aware of the child's fever before convulsions occur. However, it has been shown that mothers are very often aware of their child being unwell a few hours before the onset of fever(38,39), and that most of them can identify their child as febrile without the use of thermometer(42). Some authors, therefore, recommend starting diazepam prophylaxis at the onset of illness rather than the onset of fever(38,39). The other problem is that of compliance(41,43). It is, therefore, of utmost importance to educate, and motivate the parents to adhere to instructions and to ensure their co-operation.

It is recommended that anti-convulsant prophylaxis if used, should be continued either for 2 years or for 1 year after the last seizures, whichever period is shorter(1). Recently a suggestion of reducing the duration of therapy has been made in view of the rapid decline of recurrence risk after six months of previous seizures(16).

The decision to start prophylactic medical therapy should be made after balancing the risks and benefit. Because febrile seizures do not have an adverse effect on neurodevelopmental outcome, there is no evidence that preventing recurrences reduces the risk of epilepsy, and anticonvulsants have side effects, the treatment decisions should be based on the actual recurrence risk facing a

particular child. In certain high risk situations (e.g., in a child with an early age of onset and a family history of febrile seizures, whose seizures occurred during a low fever of short duration) or where parents are very anxious, and/or the child does not have easily accessible medical help, anticonvulsants may be advised. Continuous prophylaxis is rarely justified. Perhaps, oral or rectal diazepam (with proper instructions for use) can be made available in such cases for intermittent prophylaxis. Providing parental information and reassurance is extremely important. The benign nature and good prognosis of febrile seizures needs to be explained and emphasized.

Conclusion

Febrile seizures are common and the majority of children who experience them do well. Most outgrow the tendency to have seizures and the seizures do not cause lasting intellectual or neurologic damage. Very few children with a very high risk of recurrence need to be exposed to anticonvulsant therapy.

In such cases, treatment decisions have to be made by the physician and the family after weighing the morbidity of recurrences versus therapy, and have to be ultimately made on an individual basis.

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