REVIEW

# Assessment of febrile seizures in children

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Abstract Febrile seizures are the most common form of childhood seizures, affecting 2-5% of all children and usually appearing between 3 months and 5 years of age. Despite its predominantly benign nature, a febrile seizure (FS) is a terrifying experience for most parents. The condition is perhaps one of the most prevalent causes of admittance to pediatric emergency wards worldwide. FS, defined as either simple or complex, may be provoked by any febrile bacterial or (more usually) viral illness. No specific level of fever is required to diagnose FS. It is essential to exclude underlying meningitis in all children with FS, either clinically or, if any doubt remains, by lumbar puncture. There is no evidence, however, to support routine lumbar puncture in all children admitted with simple FS, especially when typical clinical signs of meningitis are lacking. The risk of epilepsy following FS is 1-6%. The association, however small, between FS and epilepsy may demonstrate a genetic link between FS and epilepsy rather than a cause and effect relationship. The effectiveness of prophylactic treatment with medication remains controversial. There is no evidence of the effectiveness of antipyretics in preventing future FS. Prophylactic use of paracetamol, ibuprofen or a combination of both in FS, is thus a questionable practice. There is reason to believe that children who have experienced a simple FS are overinvestigated and over-treated. This review aims to provide physicians with adequate knowledge to make rational assessments of children with febrile seizures.

Keywords Seizures · Fever · Child

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#### Introduction

Although childhood febrile seizures in most cases are benign and self-limiting [102], witnessing such seizures is a terrifying experience for most parents. Febrile seizures are the most common form of childhood seizures, affecting approximately 2–5% of children and usually occurs between 3 months and 5 years, with a peak incidence at 18 months [2, 39, 64]. The onset of FS in a child older than 6 years is unusual [102].

In a consensus report issued by the US National Institute of Health (NIH) in 1980 [31], the definition of FS is a seizure "in infancy or childhood [...] associated with fever but without evidence of intracranial infection or defined cause for the seizure". This definition excludes cases of FS in children who have previously had afebrile seizures. A modified definition of FS was issued in 1993, by the International League Against Epilepsy [5], as "an epileptic seizure occurring in childhood after the age of 1 month, associated with a febrile illness not caused by an infection of the central nervous system (CNS), without previous neonatal seizures or a previous unprovoked seizure, and not meeting criteria for other acute symptomatic seizures". This definition underlines the key diagnostic concepts in the assessment of FS: to determine whether or not the fever is caused by any potentially harmful condition, and to exclude meningitis, encephalitis, serious electrolyte imbalance, or other acute neurological illnesses, as well as prior unprovoked seizures. The diagnosis of FS implies, therefore, an evaluation of the cause of the fever, and rules out alternative causes of the seizure besides the fever per se.

Febrile seizures are usually categorized as either simple or complex [102]. A simple FS is defined as a self-limiting tonic-clonic seizure of short duration (<15 min) that does not usually recur within the next 24 h, and that does not leave

any postictal pathology. On the other hand, a complex FS is defined as having one or more of the following features:

- 1. A focal onset or focal features during the seizure, or a seizure followed by a neurological deficit
- 2. Prolonged duration (>15 min)
- 3. Recurrent seizures within the same febrile illness over a 24-h period
- 4. Previous neurological impairment, such as cerebral palsy or developmental delay [50, 67, 82, 84, 99]

Features of simple and complex febrile seizures are summarized in Table 1.

The wide range in the estimates of the prevalence of complex febrile seizures (9–35%) may reflect the diagnostic challenge of differentiating complex from simple FS, or even from afebrile seizures. Although complex febrile seizures make up a small fraction of all childhood seizures, they are commonly associated with febrile first-time convulsive status epilepticus (CSE) in children [21, 59].

There is reason to believe that despite their benign nature, simple febrile seizures are one of the most prevalent causes of admittance to pediatric emergency wards worldwide [22]. Management of simple FS might easily lead to unnecessary use of medical resources, parental fear, and restrictions in the life of the child.

This review aims at exploring the current knowledge of febrile seizures and their management, in order to equip physicians who will encounter children with ongoing or recent febrile seizures with sufficient medical knowledge. Materials and methods

Key clinical questions concerning the management of the child presenting with a seizure were used in the search strategy. Specific questions, type of question, and specific search terms (as mesh headings and text words) were defined. Medline (1966 to January 2007); Embase (1980 to January 2007), and Cochrane (up to January 2007) were searched; the searches were confined to humans aged 0-18 years, English language, and citations in references found. The references generated were sifted for relevance to the clinical questions by their titles and abstracts. Inclusion criteria were: articles that investigated the clinical questions identified; scientific literature reviews; reviews or clinical guidelines written by a national body; and large, well-designed clinical trials (RCT, matched case-control, cohort). Some retrospective cohort studies were also included. Management recommendations were made based on this literature search.

# **Risk factors**

Generally, at least 50% of children who present with FS will have no identified risk factors [102].

#### Fever

Although the definition of FS includes the presence of fever, there is no current evidence of the level of fever required to

 Table 1 Simple and complex febrile seizures

# Self-limiting

- Short duration (<15 minutes)
- Tonic-clonic features
- No reoccurrence within the next 24 hours
- No postictal pathology

Complex seizures:

Simple seizures:

- Longer duration (>15 minutes)
- May present as series of seizures with limited time interval
- New events may reoccur within the next 24 hours
- Focal seizures, with several possible features:
  - o Clonic and/or tonic movements
  - o Loss of muscle tone
  - Beginning on one side of the body, with or without secondary generalization
  - Head and/or eye deviation to one side
  - Seizure activity followed by transient unilateral paralysis (lasting minutes to hours, occasionally days)

diagnose FS [102]. Despite the common belief that the rise in temperature *per se* is more important for the development of FS than the actual temperature achieved, there is no evidence to support that view [14, 55]. Fever in children with FS is typically higher than in controls with similar fever-related illnesses, and seizures usually develop in the first 24 hours of the illness [91]. Measurements of fever have methodological problems because some reports in the literature refer to axillary temperature and some to rectal temperature, and because FS does not always occur at the peak level of fever or at the onset of fever [91]. Although the average level of fever in children with FS is high (39.8°C), the seizure itself is the first sign of febrile illness in 25–50% of all cases of FS [30].

Armon et al. [8], explored the level of fever in FS, using the Delphi technique [38], where an axillary temperature of >38°C was proposed in the first round to the Delphi panel as a diagnostic limit in FS, but no consensus was reached. In the second round, the Likert scale was modified such that actual temperatures (between 37.0°C and 38.6°C in increments of 0.1 of a degree) were given. Panelists were asked to "place one cross only in the temperature box that corresponds to the lowest recorded axillary temperature that would lead you to make a preliminary diagnosis of seizure with fever". The median and modal values were 37.8°C with a range of 37.7°C to 38.0°C and interquartile range all within the 37.8°C box. During the validation study it was clear that a simple temperature cut-off was not practical and therefore the statement was modified to allow the diagnosis of "febrile seizure" if the history and examination was indicative [8]. This decision was in accordance with the FS definition proposal developed at the NIH consensus conference in 1980 [3].

#### Concurrent infection

Any febrile viral or bacterial illness may provoke FS. Viral infections, in particular, are frequently associated with FS [63, 68]. The prevalence of bacterial infections in children presenting with FS is low; however, such infections may be serious when they do occur. Although the prevalence of meningitis is rare in the developed world, meningitis presents with seizures in 24% of children [20]. Offringa et al. [65], reported that the all-over frequency of bacterial meningitis was 7% in 309 children with FS seen in two pediatric emergency wards, with an increasing likelihood of meningitis with longer seizure durations. In a prospective population based study, Chin et al. [21] found that bacterial meningitis occurred in up to 18% of children with complex febrile seizures. Other researchers have found a lower prevalence of meningitis (0-5%) in FS populations [6, 41, 48, 62, 75, 88]. Meningitis is less likely in the absence of well-known clinical findings, such as petechiae, nuchal rigidity, altered consciousness, and coma [34, 65]. Based on data from the UK in the period 1980–1990, the population risk of meningitis (with or without seizure) is highest in children aged 1-11 months [29], although this rate has decreased since the introduction of pneumococcal and Haemophilus influenzae type B (HIB) vaccines. Trainor et al. [88] assessed the causes of infections found in children with first-time FS in a multicenter retrospective review (n=455), and found that bacteremia occurred in 1.3% of children in whom blood cultures were drawn (69% of the study population). While 34% of all cases of infection were not identified, the most commonly diagnosed infectious illnesses were otitis media (34%), upper respiratory infection (12%), viral syndrome (6%), and pneumonia (6%). Urinary tract infection (3%), gastroenteritis (2%), varicella (2%), and bronchiolitis (1%) were identified in smaller subsets of patients, while no cases of meningitis were found [88]. Other studies suggest an increased risk with exposure to infectious illnesses such as human herpes virus-6 [36], and even to routine immunization [9, 43].

## Genetics

A positive family history of FS (in first-degree relatives) is probably the most consistently identified risk factor for developing FS, and the risk increases with the number of relatives who have this history [91]. The genetic component of FS is complex, however, and the risk varies greatly between families who may have similar histories of the condition [17, 32, 66, 89]. Approximately 25–40% of children presenting with FS have a positive family history, and siblings of a child with FS have an estimated 9–22% risk of developing FS [40]. Monozygotic twins are reported to be more likely to show concordance, in this respect, than are dizygotic twins [102].

There have been reports of linkages to FS on several chromosomes, including 2q, 5q, 5, 8q, 19p, and 19q, with the strongest linkage on chromosome 2q and specifically, linkage to the genes responsible for sodium channel receptors, in particular, a mutation in the alpha (a) subunit of the first neuronal sodium channel gene [76, 81, 102]. However, no clear evidence of specific genetic loci has yet been found, and studies in this field are complicated because FS is most probably multifactorial in origin.

## Prenatal and early life exposure

Previous reports have indicated an elevated risk of developing FS in children with underlying brain disorders associated with factors such as premature birth, delayed discharge from the neonatal intensive care unit, and developmental delay. However, a causal link between these factors and FS has not yet been established [17, 35, 44, 58, 94, 95, 97], and the evidence, so far, may be hampered by selection bias, since the results vary depending on whether the research was hospital- or community-based. Vestergaard et al. [98], explored the associations between prenatal exposure to cigarette smoke, alcohol, and coffee and the risk of FS in two population-based birth cohorts. Except for smoking, these factors were not associated with the risk of FS. Even the results related to smoking were not convincing. These findings are at odds with two previous case-control studies, which found that prenatal smoking was associated with a two-fold increased risk of FS, and that the risk increased with the number of cigarettes smoked per day [15, 19]. The latter studies, however, have been the subject of methodological criticism.

#### **Treatment and diagnostics**

## Treatment of an ongoing seizure

The treatment for a simple FS, based on the assessment of an ongoing FS, is airway maintenance and abortion of the seizure in order to prevent a febrile status epilepticus. Most febrile seizures are of limited duration, lasting fewer than 10 min, and no drug intervention is usually necessary [102]. Most simple seizures end before the child reaches a physician. In prolonged attacks of FS, lasting longer than 10 min, rectal diazepam is effective, when no other acute medical care is accessible. The dose of rectal diazepam is determined by the child's age and weight and is routinely about 0.5 mg per kg (2.5 mg for children aged 6–12 months; 5 mg for 1– 4 years; 7.5 mg for 5–9 years) [54]. A pragmatic approach to doses may be needed, because, in an emergency setting, it is unlikely to be appropriate to attempt accurate weighing of a child undergoing a seizure.

In a recent multicenter, randomized controlled trial (219 separate episodes of seizure in 177 patients), McIntvre et al. [54] reported that midazolam administered via the buccal route was more effective than rectal diazepam for children presenting to hospital with acute seizures, and was not associated with an increased incidence of respiratory depression. The use of midazolam, however, is not yet a routine treatment for FS [83]. In a review from the Cochrane collaboration, Appleton et al. [7] concluded that there was some evidence that rectal lorazepam may be more effective and safer than rectal diazepam, but that the data were insufficient to indicate that lorazepam should replace diazepam as the first-choice rectal drug in treating acute tonic-clonic convulsions and convulsive status epilepticus. Despite the lack of clear evidence that the use of benzodiazepines is safe and effective when used in prehospital settings, Alldredge et al. [1] reported that prehospital administration of diazepam may shorten the duration of status epilepticus in children and simplify their subsequent management in an emergency department setting. They also considered that there were no significant differences between rectal and intravenous diazepam therapy with regard to seizure duration, the need for intubation, or recurrent seizures.

## Diagnostic work-up following FS

The main task in the diagnostic evaluation of a child with a recent attack of FS is to determine whether the fever and/or seizure result from potentially harmful or even lethal illnesses. First of all, the risk of meningitis must be considered. The estimated incidence of meningitis in children who present with an apparent FS is 2-7% [6, 41, 48, 62, 65, 75]. FS in association with meningitis often presents as complex FS [71]. Other bacterial infections, such as urinary, ear, and airways infections, must also be considered in a child with FS, although most infections associated with FS are probably of viral etiology. Malaria needs to be considered in countries where it is epidemic. A detailed history and a targeted physical examination are essential and can eliminate several serious conditions. A flow-chart of the initial assessment of FS [8, 12, 61, 88, 101, 102], is presented in Fig. 1.

The risk of epilepsy, which will be discussed in a later section, increases if the child's FS was complex rather than simple; if the child was neurologically abnormal before the first FS; and if there is a family history of epilepsy in the child's parents or siblings [71].

#### Admittance

Children with simple FS with no suspicion of serious underlying illness, who are older than 18 months, do not need to be routinely admitted to a hospital ward. This is provided that their consciousness has returned to normal, there is ready access to health care, and the parents are not overwhelmed with anxiety [12]. Although, in most cases, FS is benign, Sweeney et al. [86] found that a majority (70%) of all children with FS were admitted to hospital, but that the value of admission and of investigations, in many cases, was questionable.

The decision to admit should be individualized. Based on current knowledge and consensus among experts, criteria for admission are age younger than 18 months, lethargy beyond the postictal state, unstable clinical status, complex FS, parental anxiety and/or uncertain home situation [8]. Diagnostic uncertainty is often more common in the first event of FS than in forthcoming events, but it is important to remember that a history of previous FS does not rule out the possibility of, for example, meningitis with later FS. Any child in whom there is the slightest suspicion of meningitis should be admitted. Admittance should include an observation period of at least 2 h [12].



FEBRILE SEIZURE

Seizure management

Sign or history of serious illness:





Laboratory investigations

No laboratory tests are proven to be of particular value in the management of a child with FS, except when there are symptoms or signs indicating a significant concurrent illness [71]. In a recent evidence-based guideline, Baumer [12] suggests that a urine sample should be checked for infection in a child with simple FS, but that no other investigation is routinely indicated. Other researchers suggest a broader laboratory investigation of infections, but do not recommend routine analysis of serum electrolytes, calcium, phosphorus, complete blood count, and blood glucose, unless they are indicated by a suspicious history or physical findings [6, 33, 41, 47, 75].

In children with diarrhea and vomiting, or signs of dehydration, analysis of serum electrolytes provides valuable information [71]. Other laboratory tests that may be helpful include anticonvulsant blood levels (if the child is being treated for a seizure disorder) and blood sugar level if the child does not regain consciousness fully after the FS, especially if there is concurrent vomiting and ketosis, or if the cerebrospinal fluid (CSF) is to be examined [71].

In some cases, the key question is whether or not to perform a lumbar puncture. This should be strongly considered when the child has had at least 3 days of illness with drowsiness and vomiting; if there is a complex FS; and if there are findings of petechiae, nuchal rigidity, drowsiness, irritability or bulging fontanel [12]. In an American Academy of Pediatrics (AAP) practice parameter from 1996 for neurodiagnostic evaluation (including lumbar puncture) following a first FS, a liberal practice for children vounger than 12 months is recommended [6]. This is due to the often subtle clinical signs of meningitis in this age group. Both Joffe et al. [48] and Offringa et al. [65] argue that history and physical examination (without lumbar puncture) in many cases discriminate between children with and without meningitis. Offringa et al. [65] studied causes and features of infections in 309 children presenting with FS and reported that specific symptoms for the combination of FS and meningitis were petechiae, nuchal rigidity, coma, persistent drowsiness, ongoing convulsions, and paresis or paralysis. Children without these features very rarely had meningitis [65]. Joffe et al. [48] also reported that history and physical examination items discriminated between children with and without meningitis, and that this diagnostic approach was as sensitive as and more specific than lumbar puncture for detecting children with FS and meningitis. Most importantly, the negative predictive value of history and physical examination was 100% [48]. In a study population of 455 children admitted with FS, Trainor et al. [88] reported that 30% had cerebrospinal fluid cultures performed, but that none of these cultures grew a bacterial pathogen. Performing routine lumbar puncture in the large majority of children with ongoing antibiotic treatment, as suggested by some researchers [6, 101], on the basis of a possible masking effect on meningitis, is not necessarily indicated, as long as antibiotics are commonly inappropriately prescribed for illnesses that have a predominantly viral etiology, such as common colds [60, 70, 85].

An EEG is not usually indicated for evaluation either in a hospital or outpatient setting [6]. EEGs are probably most helpful if there is doubt about whether FS has really occurred, because EEGs carried out on the day of the seizure are abnormal in as many as 88% of patients [71].

## Prognosis

#### Recurrence

The most prevalent pathology following FS is a recurrence of FS, with an estimated risk of 29–35% [12]. The risk of recurrence depends on a complex interplay between genetic

and environmental factors. In a prospective randomized study, Knudsen [51] identified five major risk factors for recurrent FS:

- 1. Age 15 months or less at the time of the first FS
- 2. Epilepsy in first-degree relatives
- 3. Febrile convulsions in first-degree relatives
- 4. A first complex FS
- 5. Attending day nursery care

The greater the number of risk factors, the higher the recurrence rate and vice versa. The 18-month recurrence rate was 80-100% if three to five risk factors were present, 50% if two factors were identified, 25% where one factor was found, and 12% if there were no predictors [51]. In another report, Offringa et al. [66] found that young age at onset (<12 months), a history of febrile or unprovoked seizure in a first-degree relative, and a rectal temperature of less than 40°C at the time of the febrile seizure were associated with a significantly increased recurrence rate. Age at 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) [42]. It is suggested that the higher recurrence risk associated with early age at onset may indicate increased vulnerability to FS or may simply be a function of the greater remaining risk period available in which to have a recurrence [82]. The recurrence hazard is highest in the first 6 to 12 months after an initial attack of FS [66].

## Epilepsy

Most children with febrile seizures, approximately 97%, never develop epilepsy. However, all studies have shown that children with FS are at increased risk of subsequent epilepsy, compared with healthy controls [12, 56]. The risk of epilepsy following a simple FS is 1-2.4%, while the risk of epilepsy following a complex FS is 4.1-6% [12]. A history of febrile convulsions is present in 10-15% of people with epilepsy or unprovoked seizure, which is several times higher than the 2-4% seen in the general population [37]. In the US community-based National Cooperative Perinatal Project [56, 57], three independent risk factors for later epilepsy following FS were identified:

- 1. Idiopathic or genetic forms of epilepsy in a first-degree relative
- 2. Abnormal neurological or developmental status before the attack of FS
- 3. Complex FS

It is suggested that the association, however small, between FS and epilepsy demonstrates a genetic link between febrile seizures and epilepsy rather than a cause and effect relationship [16, 49].

#### Neurological deficits

It is not yet quite clear whether children with a history of FS are at greater risk of developing neurological deficits. However, most population-based studies have shown no obvious association between simple or complex FS, including febrile status, and the later development of neurological deficits, overall cognitive functioning, or specific memory impairment [25, 95, 96]. On the other hand, Wallace [100] studied children with febrile seizures who were admitted to hospital and found that about 5% of them acquired new neurological abnormalities. Schiottz-Christensen et al. [77] studied 14 pairs of monozygous twins discordant with regard to febrile seizures, and found an increased incidence of "soft signs" and behavioral disturbances among twins who had experienced an FS, but whether these may have preceded the seizures is questionable. In the same population, significant intellectual impairments in those who had suffered febrile seizures were found, although the deficits were small [78].

## Mortality

The mortality associated with FS is extremely low. No deaths were reported from the National Collaboration Perinatal Project [56, 57], or from the British cohort study [6, 95].

Prognostic risks following a first event of FS are summarized in Table 2.

## Prevention

Despite the widespread use of antipyretic medication during fever in children who have experienced FS [23], there is little evidence that antipyretics reduce the risk of recurrence of FS [18, 74]. Van Stuijvenberg et al. [92], evaluated the effect of ibuprofen syrup versus placebo during fever in children aged 1–4 years who had a minimum of one risk factor for FS. Median follow-up time was 12 months. The relative risk of recurrence in the group receiving ibuprofen was not significantly different from that in the placebo group [92]. Thus, the practice of using "round the clock" ibuprofen is

Table 2 Prognosis after first febrile seizure

Pathology	Risk percentage (%)
Risk of reoccurrence (total)	29–35
If age of onset <1 year	≈50
If age of onset $>3$ years	$\approx 20$
Risk of epilepsy after simple febrile seizure	1-2.4
Risk of epilepsy after complex febrile seizure	4.1-6
Neurological deficits	0–5

not, so far, supported by research and may even contribute to parental fever phobia [10]. Also, there is still no evidence that antipyretics will prevent further febrile seizures in combination with low doses of diazepam [26, 90]. In an AAP practice parameter from 2000 [11], it is concluded that "although antipyretic agents may improve the comfort of the child, they will not prevent febrile seizures".

Previous reports indicate the effects of both valproate and phenobarbital in reducing the recurrence of FS compared with placebo [10, 69]. The significant side effects of these drugs, however, limit their practical use. In fact, Farwell et al. [27] concluded that phenobarbital depresses cognitive performance in children treated for FS and that this disadvantage, which may outlast the administration of the drug by several months, is not offset by the benefit of seizure prevention. In an attempt to avoid the side effects of continuous administration, phenobarbital has been given for a limited period after onset of fever, but this has proven ineffective [62]. This is probably due to the delay in achieving appropriate serum and tissue levels. Both the Royal College of Pediatrics and Child Health [4] and the American Academy of Pediatrics [11] do not recommend the use of prophylactic antiepileptic medication in children with either simple or complex FS.

Carbamazepine and phenytoin have been found to be ineffective in the short- and long-term management of FS [10].

There is conflicting evidence on the effectiveness of prophylactic treatment with diazepam for the recurrence of FS. Nevertheless, the majority opinion is that such treatment is likely to be effective [11, 52, 72]. The decision on whether to initiate benzodiazepine prophylaxis depends on factors such as drug adverse effects, the frequency and type of FS, access to medical treatment, and the capabilities and wishes of carers [102]. An important disadvantage of early (preseizure) administration of oral [72] or rectal [53] diazepam is drowsiness and ataxia in the child, which may confuse medical judgment with regard to serious febrile illnesses, like meningitis or encephalitis. Several researchers suggest that if a child appears to have a very low threshold for FS with any febrile episode, and particularly if the seizures are recurrent and prolonged, it is appropriate to administer rectal diazepam either whenever the child is febrile and before seizure starts [51, 72], or as soon as the seizure starts [102]. Baumer et al. [12] conclude that if parental anxiety associated with FS is severe, intermittent oral diazepam at the onset of febrile illness may be justified for the effective prevention of recurrence.

## **Parent information**

Many parents (or other carers), faced for the first time with an FS, may believe that the child is dying [13]. Thus, FS may cause serious anxiety and fear [13, 80], and fever phobia [93] among carers, despite the good prognosis. High levels of anxiety are more often found in parents with little or no knowledge of FS and with a low level of education [28].

In a study from The Netherlands, van Stuijvenberg et al. [93] studied parents' perceptions and knowledge of fever and FS, and concluded that parental fear of fever and FS was a major problem, with several negative consequences for daily family life. Adequate provision of information seemed to reduce parental fear [93].

Despite the medical obligation to provide good information, its effectiveness in relation to FS is unclear. Flury et al. [28] reported that even in parents with a knowledge of FS, anxiety levels were very high, and parents would still react inappropriately in the case of recurrence. Therefore, information provided to parents must be specific, especially about which measures to take or which to avoid [28].

For the majority of children with FS, parental education and counseling will be the sole treatment. Adequate information on the nature and prognosis of FS should be provided and repeated. The amount and level of information will depend on the parents' anxiety level, education and ability to pay attention to the information given at that particular time.

In those cases for which prophylactic treatment with diazepam is recommended, careful instructions regarding its use must be provided and most probably repeated. It is usually advisable to see these parents after a few weeks to review the information given and to answer any additional questions.

There is no evidence that admitting a child to hospital after an attack of FS merely to reassure parents has any benefit [73].

#### Conclusions

Febrile seizures are the most common form of seizures seen in children; their predominantly benign nature is demonstrated in all research in this field, but a small minority of children presenting with FS will develop epilepsy.

Febrile seizures are provoked by fever and usually develop within the first 24 h of the febrile illness. No specific level of fever is required to diagnose FS. Despite the commonly held belief that the rise in fever *per se* is the main risk factor for developing seizures, there is still no evidence to support this view. There is, as yet, no evidence of the effectiveness of antipyretics in preventing future febrile seizures [24, 26, 52, 87].

The main task in the initial assessment of FS is the first-aid management of an ongoing seizure, and then to exclude serious medical illnesses that may have caused the fever. There is reason to believe that children who have experienced a simple FS are over-admitted, over-investigated, and over-treated [23]. Medical staff are responsible for providing sufficient medical information to parents, in order to reduce

irrational fear and unnecessary use of health resources. However, children should be admitted if they are younger than 18 months; or if they have lethargy beyond the postictal state, unstable clinical status, or complex FS; or where there is parental anxiety and/or an uncertain home situation.

Indications for lumbar puncture in children with FS are controversial and clinicians have little evidence on which to base their decision. This may lower the clinical threshold for performing a lumbar puncture, in an attempt to reduce uncertainty in diagnosis. Based on current knowledge, there seems to be no need for the routine investigation of cerebrospinal fluid in children admitted with FS who are more than 12 months old and who do not have any apparent signs of meningitis.

When the diagnosis of simple FS is reached, the main target strategy should be reassurance and explanation to parents. The parents of children who experience febrile seizures often lack knowledge, and have heightened concerns and inadequate first-aid management skills [79]. The literature recognizes the importance of parental education in the management of children with simple FS [45, 46, 93], but the effectiveness of such education is questionable [28]. An understanding of the nature and prognosis of FS will help the physician to provide adequate medical care for children with this condition, to reassure parents, and to avoid unnecessary diagnostic and therapeutic interventions.

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## References

- Alldredge BK, Wall DB, Ferriero DM (1995) Effect of prehospital treatment on the outcome of status epilepticus in children. Pediatr Neurol 12:213–216
- Annegers JF, Hauser WA, Shirts SB, Kurland LT (1987) Factors prognostic of unprovoked seizures after febrile convulsions. N Engl J Med 316:493–498
- Anonymous (1980) Consensus statement. Febrile seizures: longterm management of children with fever-associated seizures. Pediatrics 66:1009–1012
- Anonymous (1991) Guidelines for the management of convulsions with fever. Joint Working Group of the Research Unit of the Royal College of Physicians and the British Paediatric Association. BMJ 303:634–636
- Anonymous (1993) Guidelines for epidemiologic studies on epilepsy. Commission on Epidemiology and Prognosis, International League against Epilepsy. Epilepsia 34:592–596
- Anonymous (1996) Practice parameter: the neurodiagnostic evaluation of the child with a first simple febrile seizure. American Academy of Pediatrics. Provisional Committee on Quality Improvement, Subcommittee on Febrile Seizures. Pediatrics 97:769–772; discussion 773–765
- Appleton R, Martland T, Phillips B (2002) Drug management for acute tonic-clonic convulsions including convulsive status epilepticus in children. Cochrane Database Syst Rev:CD001905

- Armon K, Stephenson T, MacFaul R, Hemingway P, Werneke U, Smith S (2003) An evidence and consensus based guideline for the management of a child after a seizure. Emerg Med J 20:13–20
- Barlow WE, Davis RL, Glasser JW, Rhodes PH, Thompson RS, Mullooly JP, Black SB, Shinefield HR, Ward JI, Marcy SM, DeStefano F, Chen RT, Immanuel V, Pearson JA, Vadheim CM, Rebolledo V, Christakis D, Benson PJ, Lewis N (2001) The risk of seizures after receipt of whole-cell pertussis or measles, mumps, and rubella vaccine. N Engl J Med 345:656–661
- Baumann RJ (1999) Technical report: treatment of the child with simple febrile seizures. Pediatrics 103:e86
- Baumann RJ, Duffner PK (2000) Treatment of children with simple febrile seizures: the AAP practice parameter. American Academy of Pediatrics. Pediatr Neurol 23:11–17
- Baumer JH (2004) Evidence based guideline for post-seizure management in children presenting acutely to secondary care. Arch Dis Child 89:278–280
- Baumer JH, David TJ, Valentine SJ, Roberts JE, Hughes BR (1981) Many parents think their child is dying when having a first febrile convulsion. Dev Med Child Neurol 23:462–464
- Berg AT (1992) Febrile seizures and epilepsy: the contributions of epidemiology. Paediatr Perinat Epidemiol 6:145–152
- Berg AT, Shinnar S, Shapiro ED, Salomon ME, Crain EF, Hauser WA (1995) Risk factors for a first febrile seizure: a matched case-control study. Epilepsia 36:334–341
- Berkovic SF, Howell RA, Hay DA, Hopper JL (1994) Epilepsies in twins. In: Wolf P (ed) Epileptic seizures and syndromes. Libbey, London, pp 157–164
- Bethune P, Gordon K, Dooley J, Camfield C, Camfield P (1993) Which child will have a febrile seizure? Am J Dis Child 147:35–39
- Camfield PR, Camfield CS, Shapiro SH, Cummings C (1980) The first febrile seizure—antipyretic instruction plus either phenobarbital or placebo to prevent recurrence. J Pediatr 97:16–21
- Cassano PA, Koepsell TD, Farwell JR (1990) Risk of febrile seizures in childhood in relation to prenatal maternal cigarette smoking and alcohol intake. Am J Epidemiol 132:462–473, discussion 474–468
- Chang YC, Guo NW, Wang ST, Huang CC, Tsai JJ (2001) Working memory of school-aged children with a history of febrile convulsions: a population study. Neurology 57:37–42
- Chin RF, Neville BG, Scott RC (2005) Meningitis is a common cause of convulsive status epilepticus with fever. Arch Dis Child 90:66–69
- Depiero AD, Teach SJ (2001) Febrile seizures. Pediatr Emerg Care 17:384–387
- Dunlop S, Taitz J (2005) Retrospective review of the management of simple febrile convulsions at a tertiary paediatric institution. J Paediatr Child Health 41:647–651
- El Bashir H, Laundy M, Booy R (2003) Diagnosis and treatment of bacterial meningitis. Arch Dis Child 88:615–620
- Ellenberg JH, Nelson KB (1978) Febrile seizures and later intellectual performance. Arch Neurol 35:17–21
- 26. El-Radhi AS, Barry W (2003) Do antipyretics prevent febrile convulsions? Arch Dis Child 88:641–642
- Farwell JR, Lee YJ, Hirtz DG, Sulzbacher SI, Ellenberg JH, Nelson KB (1990) Phenobarbital for febrile seizures—effects on intelligence and on seizure recurrence. N Engl J Med 322:364–369
- Flury T, Aebi C, Donati F (2001) Febrile seizures and parental anxiety: does information help? Swiss Med Wkly 131:556–560
- 29. Fortnum HM, Davis AC (1993) Epidemiology of bacterial meningitis. Arch Dis Child 68:763–767
- Freedman SB, Powell EC (2003) Pediatric seizures and their management in the emergency department. Clin Pediatr Emerg Med 4:195–206
- Freeman JM (1980) Febrile seizures: a consensus of their significance, evaluation, and treatment. Pediatrics 66:1009

- Fukuyama Y, Kagawa K, Tanaka K (1979) A genetic study of febrile convulsions. Eur Neurol 18:166–182
- Gerber MA, Berliner BC (1981) The child with a 'simple' febrile seizure. Appropriate diagnostic evaluation. Am J Dis Child 135: 431–433
- 34. Green SM, Rothrock SG, Clem KJ, Zurcher RF, Mellick L (1993) Can seizures be the sole manifestation of meningitis in febrile children? Pediatrics 92:527–534
- 35. Greenwood R, Golding J, Ross E, Verity C (1998) Prenatal and perinatal antecedents of febrile convulsions and afebrile seizures: data from a national cohort study. Paediatr Perinat Epidemiol 12 (Suppl 1):76–95
- 36. Hall CB, Long CE, Schnabel KC, Caserta MT, McIntyre KM, Costanzo MA, Knott A, Dewhurst S, Insel RA, Epstein LG (1994) Human herpesvirus-6 infection in children. A prospective study of complications and reactivation. N Engl J Med 331:432–438
- Hamati-Haddad A, Abou-Khalil B (1998) Epilepsy diagnosis and localization in patients with antecedent childhood febrile convulsions. Neurology 50:917–922
- Hasson F, Keeney S, McKenna H (2000) Research guidelines for the Delphi survey technique. J Adv Nurs 32:1008–1015
- Hauser WA (1994) The prevalence and incidence of convulsive disorders in children. Epilepsia 35(Suppl 2):S1–S6
- Hauser WA, Annegers JF, Anderson VE, Kurland LT (1985) The risk of seizure disorders among relatives of children with febrile convulsions. Neurology 35:1268–1273
- Heijbel J, Blom S, Bergfors PG (1980) Simple febrile convulsions. A prospective incidence study and an evaluation of investigations initially needed. Neuropadiatrie 11:45–56
- Hirtz DG (1989) Generalized tonic-clonic and febrile seizures. Pediatr Clin North Am 36:365–382
- Hirtz DG, Nelson KB, Ellenberg JH (1983) Seizures following childhood immunizations. J Pediatr 102:14–18
- 44. Huang CC, Wang ST, Chang YC, Huang MC, Chi YC, Tsai JJ (1999) Risk factors for a first febrile convulsion in children: a population study in southern Taiwan. Epilepsia 40:719–725
- 45. Huang MC, Liu CC, Chi YC, Huang CC, Cain K (2001) Parental concerns for the child with febrile convulsion: longterm effects of educational interventions. Acta Neurol Scand 103:288–293
- Huang MC, Liu CC, Huang CC, Thomas K (2002) Parental responses to first and recurrent febrile convulsions. Acta Neurol Scand 105:293–299
- Jaffe M, Bar-Joseph G, Tirosh E (1981) Fever and convulsions indications for laboratory investigations. Pediatrics 67:729–731
- Joffe A, McCormick M, DeAngelis C (1983) Which children with febrile seizures need lumbar puncture? A decision analysis approach. Am J Dis Child 137:1153–1156
- Kajitani T, Kimura T, Sumita M, Kaneko M (1992) Relationship between benign epilepsy of children with centro-temporal EEG foci and febrile convulsions. Brain Dev 14:230–234
- Karande S (2007) Febrile seizures: a review for family physicians. Indian J Med Sci 61:161–172
- Knudsen FU (1985) Recurrence risk after first febrile seizure and effect of short term diazepam prophylaxis. Arch Dis Child 60: 1045–1049
- 52. Knudsen FU (2000) Febrile seizures: treatment and prognosis. Epilepsia 41:2–9
- Knudsen FU, Vestermark S (1978) Prophylactic diazepam or phenobarbitone in febrile convulsions: a prospective, controlled study. Arch Dis Child 53:660–663
- 54. McIntyre J, Robertson S, Norris E, Appleton R, Whitehouse WP, Phillips B, Martland T, Berry K, Collier J, Smith S, Choonara I (2005) Safety and efficacy of buccal midazolam versus rectal diazepam for emergency treatment of seizures in children: a randomised controlled trial. Lancet 366:205–210

- Minchom PE, Wallace SJ (1984) Febrile convulsions: electroencephalographic changes related to rectal temperature. Arch Dis Child 59:371–373
- Nelson KB, Ellenberg JH (1976) Predictors of epilepsy in children who have experienced febrile seizures. N Engl J Med 295:1029–1033
- Nelson KB, Ellenberg JH (1978) Prognosis in children with febrile seizures. Pediatrics 61:720–727
- Nelson KB, Ellenberg JH (1990) Prenatal and perinatal antecedents of febrile seizures. Ann Neurol 27:127–131
- Neville BG, Chin RF, Scott RC (2007) Childhood convulsive status epilepticus: epidemiology, management and outcome. Acta Neurol Scand 115:21–24
- O'Brien KL, Dowell SF, Schwartz B, Marcy SM, Phillips WR, Gerber MA (1998) Cough illness/bronchitis: principles of judicious use of antimicrobial agents. Pediatrics 101:S178–S181
- Offringa M, Moyer VA (2001) Evidence based Pediatrics: evidence based management of seizures associated with fever. BMJ 323: 1111–1114
- Offringa M, Moyer VA (2001) An evidence-based approach to managing seizures associated with fever in children. West J Med 175:254–259
- Offringa M, Kroes AC, Derksen-Lubsen G (1990) Viral infections in febrile seizures. J Pediatr 117:510–511
- 64. Offringa M, Hazebroek-Kampschreur AA, Derksen-Lubsen G (1991) Prevalence of febrile seizures in Dutch schoolchildren. Paediatr Perinat Epidemiol 5:181–188
- 65. Offringa M, Beishuizen A, Derksen-Lubsen G, Lubsen J (1992) Seizures and fever: can we rule out meningitis on clinical grounds alone? Clin Pediatr (Phila) 31:514–522
- 66. Offringa M, Bossuyt PM, Lubsen J, Ellenberg JH, Nelson KB, Knudsen FU, Annegers JF, el-Radhi AS, Habbema JD, Derksen-Lubsen G, et al. (1994) Risk factors for seizure recurrence in children with febrile seizures: a pooled analysis of individual patient data from five studies. J Pediatr 124:574–584
- 67. Piperidou HN, Heliopoulos IN, Maltezos ES, Stathopoulos GA, Milonas IA (2002) Retrospective study of febrile seizures: subsequent electroencephalogram findings, unprovoked seizures and epilepsy in adolescents. J Int Med Res 30:560–565
- Rantala H, Uhari M, Tuokko H (1990) Viral infections and recurrences of febrile convulsions. J Pediatr 116:195–199
- Rantala H, Tarkka R, Uhari M (1997) A meta-analytic review of the preventive treatment of recurrences of febrile seizures. J Pediatr 131:922–925
- Rosenstein N, Phillips WR, Gerber MA, Marcy M, Schwartz B, Dowell SF (1998) The common cold—principles of judicious use of microbial agents. Pediatrics 101:S181–S184
- Rosman NP (2003) Evaluation of the child who convulses with fever. Paediatr Drugs 5:457–461
- Rosman NP, Colton T, Labazzo J, Gilbert PL, Gardella NB, Kaye EM, Van Bennekom C, Winter MR (1993) A controlled trial of diazepam administered during febrile illnesses to prevent recurrence of febrile seizures. N Engl J Med 329:79–84
- 73. Rosser WW (2005) Fever and common childhood infections. In: Jones R, Britten N, Culpepper L, Gass D, Grol R, Mant D, Silagy C (eds) Oxford textbook of primary medical care. Oxford University Press, Oxford
- 74. Rutter N, Metcalfe DH (1978) Febrile convulsions-what do parents do? Br Med J 2:1345–1346
- Rutter N, Smales OR (1977) Role of routine investigations in children presenting with their first febrile convulsion. Arch Dis Child 52:188–191
- Scheffer IE, Berkovic SF (1997) Generalized epilepsy with febrile seizures plus. A genetic disorder with heterogeneous clinical phenotypes. Brain 120(Pt 3):479–490
- Schiottz-Christensen E (1973) Neurological findings in twins discordant for febrile convulsions. Acta Neurol Scand 49:368–378

- Schiottz-Christensen E, Bruhn P (1973) Intelligence, behaviour and scholastic achievement subsequent to febrile convulsions: an analysis of discordant twin-pairs. Dev Med Child Neurol 15: 565–575
- Shinnar S, Glauser TA (2002) Febrile seizures. J Child Neurol 17 (Suppl 1):S44–S52
- Shuper A, Gabbay U, Mimouni M (1996) Parental anxiety in febrile convulsions. Isr J Med Sci 32:1282–1285
- Singh R, Scheffer IE, Crossland K, Berkovic SF (1999) Generalized epilepsy with febrile seizures plus: a common childhood-onset genetic epilepsy syndrome. Ann Neurol 45:75–81
- Singhi PD, Srinivas M (2001) Febrile seizures. Indian Pediatr 38:733–740
- Srinivasan J, Wallace KA, Scheffer IE (2005) Febrile seizures. Aust Fam Physician 34:1021–1025
- Stenklyft PH, Carmona M (1994) Febrile seizures. Emerg Med Clin North Am 12:989–999
- 85. Straand J, Rokstad KS, Sandvik H (1998) Prescribing systemic antibiotics in general practice. A report from the More & Romsdal Prescription Study. Scand J Prim Health Care 16:121–127
- 86. Sweeney A, Gibbs J, Monteil F, Appleton R, Choonara I (1996) The management of febrile seizures in the Mersey Region. Dev Med Child Neurol 38:578–584
- Thoman JE, Duffner PK, Shucard JL (2004) Do serum sodium levels predict febrile seizure recurrence within 24 hours? Pediatr Neurol 31:342–344
- Trainor JL, Hampers LC, Krug SE, Listernick R (2001) Children with first-time simple febrile seizures are at low risk of serious bacterial illness. Acad Emerg Med 8:781–787
- Tsuboi T, Okada S (1985) Exogenous causes of seizures in children: a population study. Acta Neurol Scand 71:107–113
- Uhari M, Rantala H, Vainionpaa L, Kurttila R (1995) Effect of acetaminophen and of low intermittent doses of diazepam on prevention of recurrences of febrile seizures. J Pediatr 126:991–995
- Van Esch A, Steyerberg EW, van Duijn CM, Offringa M, Derksen-Lubsen G, van Steensel-Moll HA (1998) Prediction of febrile seizures in siblings: a practical approach. Eur J Pediatr 157:340–344
- 92. Van Stuijvenberg M, Derksen-Lubsen G, Steyerberg EW, Habbema JD, Moll HA (1998) Randomized, controlled trial of ibuprofen syrup administered during febrile illnesses to prevent febrile seizure recurrences. Pediatrics 102:E51
- 93. Van Stuijvenberg M, de Vos S, Tjiang GC, Steyerberg EW, Derksen-Lubsen G, Moll HA (1999) Parents' fear regarding fever and febrile seizures. Acta Paediatr 88:618–622
- 94. Verity CM, Butler NR, Golding J (1985) Febrile convulsions in a national cohort followed up from birth. II. Medical history and intellectual ability at 5 years of age. Br Med J (Clin Res Ed) 290: 1311–1315
- 95. Verity CM, Butler NR, Golding J (1985) Febrile convulsions in a national cohort followed up from birth. I. Prevalence and recurrence in the first five years of life. Br Med J (Clin Res Ed) 290:1307–1310
- 96. Verity CM, Greenwood R, Golding J (1998) Long-term intellectual and behavioral outcomes of children with febrile convulsions. N Engl J Med 338:1723–1728
- Vestergaard M, Basso O, Henriksen TB, Ostergaard JR, Olsen J (2002) Risk factors for febrile convulsions. Epidemiology 13: 282–287
- Vestergaard M, Wisborg K, Henriksen TB, Secher NJ, Ostergaard JR, Olsen J (2005) Prenatal exposure to cigarettes, alcohol, and coffee and the risk for febrile seizures. Pediatrics 116:1089–1094
- 99. Wadhwa N, Bharucha B, Chablani U, Contractor N (1992) An epidemiological study of febrile seizures with special reference

to family history and HLA linkage. Indian Pediatr 29:1479-1485

- 100. Wallace SJ (1976) Neurological and intellectual deficits: convulsions with fever viewed as acute indications of life-long developmental defects. In: Brazier MAB, Coceani F (eds) Brain dysfunction in infantile febrile convulsions. Raven, New York, pp 259–277
- 101. Warden CR, Zibulewsky J, Mace S, Gold C, Gausche-Hill M (2003) Evaluation and management of febrile seizures in the outof-hospital and emergency department settings. Ann Emerg Med 41:215–222
- Waruiru C, Appleton R (2004) Febrile seizures: an update. Arch Dis Child 89:751–756