Febrile convulsions – a practical guide

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Introduction

Febrile convulsions present the most common problem in paediatric neurology. How serious are they for the child? Opinions have changed with time. In 1949 Lennox wrote: 'febrile convulsions may cause brain pathology as evidenced by transient or permanent neurological deficit'. In contrast, in 1991 Robinson referred to children with febrile convulsions as having a 'generally excellent prognosis'[1].

Why has there been this change in opinion? One reason is that earlier reports of the relatively poor prognosis of children with more severe problems attending specialised clinics or hospital have been balanced by the more optimistic findings of population-based studies of less selected groups of children[2-16]. Another reason is that the results of studies depend on the way febrile convulsions are defined – some researchers have included children with underlying meningitis or encephalitis in their studies of febrile convulsions. The issues have been discussed in recent reviews[17-20].

It is now recognised that in a small number of children febrile convulsions are the first sign that the child has an inherited seizure disorder that includes afebrile as well as febrile seizures.

Definitions

In this text febrile convulsion is used synonymously with febrile seizure.

Febrile convulsions
It has become generally accepted that seizures known to be symptomatic of an underlying infection should not be called febrile convulsions. The Commission on Epidemiology and Prognosis of the International League Against Epilepsy[21] defined a febrile convulsion as:

'an epileptic seizure ... occurring in childhood after age one month, associated with a febrile illness not caused by an infection of the CNS, without previous neonatal seizures or a previous unprovoked seizure, and not meeting criteria for other acute symptomatic seizures'.

Simple versus complex febrile convulsions
Febrile convulsions can be sub-classified. In the National Collaborative Perinatal Project (NCPP), the large American prospective population study[9], *complex* febrile convulsions (seizures) were defined as those that had one or more of the following:

- Duration more than 15 minutes
- Recurrence within 24 hours
- Focal features.

Febrile convulsions that did not have complex features were *simple*. Other studies have adopted very similar definitions, however Hesdorffer et al found that the distribution of first febrile seizure duration was best modelled by assuming two populations and their data suggested that ten minutes should be the upper limit for a simple febrile seizure[22].

Febrile status epilepticus
Defined as a febrile convulsion lasting 30 minutes or more or a series of febrile convulsions without full return to consciousness during that period.

Incidence, prevalence and recurrence

Overall rates
Between 2 and 4% of all children have one or more febrile convulsions by the age of five years. Some studies find higher rates in boys than in girls but others do not. In America Nelson and Ellenberg[10] reported racial differences – the prevalence rates being 3.5% of white and 4.2% of black children. There are geographical differences – e.g. a prevalence of 8.3% by three years of age in Tokyo[23] and an incidence rate of 6.9% at age four years in Finland[24].

Age
Febrile convulsions most commonly start in the second year of life. Children are at greatest risk between six months and three years of age[19]. The age of onset has been reported to vary between two months of age and seven years nine months[14].

Type of febrile convulsion
Population-based studies that include children who are not admitted to hospital have found that the following proportions of first febrile convulsions are complex – 18% in America[9], 22% in Britain[14] and 8.6% in Scandinavia[5].

Febrile recurrences
'Recurrence' in this context means more than one episode of febrile convulsions, as opposed to 'multiple' which means more than one convulsion during an episode of fever. Berg et al[25] performed a meta-analysis and found that the overall risk of a recurrence was 34.3%. Young age at onset (one year or less) and a family history of febrile seizures predicted increased risk. Focal, prolonged and multiple convulsions were only associated with a small increase. Other studies have found similar results. Most recurrences occur within three years of the first[19].

Aetiology

Genetic factors
There is an expanding literature on the genetics of febrile convulsions. Population-based studies suggest that family history is important and that febrile convulsions and epilepsy each provide an independent contribution to the familial risk of febrile convulsions[26,27]. Forsgren[6] concluded that multifactorial inheritance was most likely. However family studies have shown that simple febrile seizures may be inherited as an autosomal dominant trait with high penetrance[28] and also show an occurrence rate ranging from 10% to 46% in children with a positive family history of febrile convulsions[29]. It seems clear that febrile convulsions make up an extremely heterogeneous group for which there is no single mode of inheritance. Causative genes have not been identified in most patients with febrile convulsions; however population-based studies have shown at least one positive association with febrile convulsions for 14 of 41 investigated genes[29]. Mutations in the voltage-gated sodium channel alpha-1, alpha-2 and beta-1 subunit genes (SCN1A, SCN2A and SCN1B) and the GABA(A) receptor gamma-2 subunit gene (GABRG2) have been identified in families with 'generalised epilepsy with febrile seizures plus' (GEFS+)[30]. Patients with GEFS+ can have febrile seizures followed by afebrile (often generalised) seizures[31]. There is evidence that the

well-recognised syndrome of epilepsy, hippocampal sclerosis and febrile convulsions is associated with common genetic variation around the SCN1A gene[32].

Prenatal factors
Maternal ill-health, parental sub-fertility[19], prenatal maternal cigarette smoking[26] and alcohol intake have been associated with the occurrence of febrile convulsions in the offspring. However, population-based studies do not find much evidence that social and maternal factors are significant[7,13,26].

Perinatal factors
A hospital-based series suggested that an abnormal pregnancy or birth history predisposes to febrile convulsions in general and complicated initial febrile convulsions in particular[19]. In contrast the population-based American NCPP[26] found that pregnancy and birth factors contributed little to the risk of febrile convulsions.

Precipitating factors
The height or duration of the fever may be important but there are problems in evaluating the temperature recordings because febrile convulsions usually occur randomly at home. Viral infections commonly cause the fever that is associated with febrile convulsions. Synthesis of immunoglobulin in the CSF of children with febrile convulsions has been demonstrated, suggesting that encephalitis may sometimes occur and not be recognised[19]. There is evidence that human herpes virus-6 (HHV-6) is linked with exanthem subitum, a condition that is frequently complicated by febrile convulsions[33]. More recent work suggests that acute HHV-6 infection is a frequent cause of febrile convulsions in young children that do not have the signs of exanthem subitum[34]. HHV-6B infection has been shown to be commonly associated with febrile status epilepticus, HHV-7 less frequently so. Together they accounted for one-third of the cases in a study of febrile status epilepticus, a condition associated with an increased risk of both hippocampal injury and subsequent temporal lobe epilepsy[35].

Bacterial infections may be associated with febrile convulsions – urinary tract infections, shigella and pneumococcal bacteraemia, for instance. Children with bacterial meningitis sometimes have convulsions and it is important to remember this when deciding whether or not to perform a lumbar puncture.

It has been shown that there are increased risks of febrile seizures on the day of receipt of DPT vaccine and 8–14 days after MMR vaccine, apparently not associated with long-term adverse consequences[36]. A study in the UK found that 6–11 days after MMR vaccine there was an increased risk of complex febrile convulsions lasting more than 30 minutes[37]. However, a Danish study found that the increased risk of febrile convulsions after MMR vaccination was small and transient. Also the long-term rate of epilepsy was not increased in children who had febrile convulsions following MMR vaccination compared with children who had febrile convulsions of a different aetiology[38].

Outcome after febrile convulsions

In 1971 Taylor and Ounsted[39] wrote: 'We think that the convulsive hypoxia sustained during prolonged febrile convulsions causes the death of vulnerable neurones in the cerebellum, the thalamus, and in mesial temporal structures'.

Evidence that febrile convulsions may cause hippocampal sclerosis or other neuronal damage

Human pathology: post-mortem studies. There are reports of neuronal necrosis in the brains of children who died after prolonged 'febrile convulsions'[40]. The neuronal necrosis is described as particularly involving cerebral cortex, the hippocampi and the cerebellum[41]. These authors were describing extreme cases that were far from typical of the majority of febrile convulsions.

Retrospective study of patients with temporal lobe epilepsy. Falconer et al[42] reported on the pathological findings in the resected temporal lobes of 100 adults with refractory temporal lobe epilepsy. About half had 'mesial temporal sclerosis' which varied from loss of nerve cells in the Sommer (H1) sector of the hippocampus to wider involvement of the temporal lobe. In 40% of the patients with mesial temporal sclerosis there was a history of 'infantile convulsions', suggesting a causal relationship.

Imaging studies. Radiological studies (pneumoencephalograms and CT scans) have shown brain swelling and then atrophy in children (some of whom were febrile) after episodes of status epilepticus[43]. More recently studies using MRI scans have reported similar findings in the hippocampus after prolonged and focal febrile seizures[44,45] and after febrile status epilepticus[46].

Kuks et al[47] studied 107 patients with drug resistant epilepsy using high-resolution volumetric MRI. Of these patients 45 had focal or diffuse hippocampal volume loss and there was a strong association between hippocampal sclerosis and a history of childhood febrile convulsions. The authors pointed out that this association does not prove a causal relationship and that 64% of their patients with hippocampal volume loss gave no history of febrile convulsions, so if childhood febrile convulsions cause some cases of hippocampal sclerosis this cannot be the only mechanism.

Scott et al[48] performed diffusion-weighted magnetic resonance studies and found evidence of early vasogenic oedema after febrile convulsions. They concluded that their findings were most consistent with a pre-existing hippocampal abnormality predisposing to febrile convulsions. A Finnish MR study showed that the occurrence of mesial temporal sclerosis after prolonged febrile seizures was uncommon[49]. A prospective study in the United States found that after febrile status epilepticus (lasting 30 minutes or more) 11.5% of cases had definitely or equivocally abnormal increased T2 signal in MRI scans of the hippocampus compared with none in the control group. A substantial number also had abnormalities in hippocampal development. A follow-up study of this group found evidence that the hippocampal T2 hyperintensity represents acute injury often evolving to a radiological appearance of hippocampal sclerosis after one year[50].

Studies of outcome after febrile convulsions

Deaths
Two large population-based studies found no deaths that were directly attributable to febrile convulsions[10,15]. The rate partly depends on how febrile convulsions are defined – some studies have included seizures complicating known meningitis or encephalitis. A Danish population-based study showed that long-term mortality was not increased in children with febrile seizures, but there seemed to be a small excess mortality during the two years after complex febrile seizures. This finding was partly explained by pre-existing neurological abnormalities and subsequent epilepsy. They concluded that parents should be reassured that death after febrile seizures is very rare, even in high-risk children[51].

Subsequent afebrile seizures

Incidence. In hospital-based series rates of subsequent afebrile seizures and/or epilepsy (defined as 'recurrent' afebrile seizures) have varied from 7% to 40%[19]. In the population-based American NCPP the rate of epilepsy after febrile convulsions was 2% by seven years of age[9] and in the British CHES[14] it was 2.5% by ten years. There is evidence that up to 85% of afebrile seizures occur within four years of febrile convulsions[19] but it seems that determination of the true incidence of afebrile seizures requires long follow up. Annegers et al[2] found that the risk of 'unprovoked seizures' after febrile convulsions steadily increased with age – 2% at five years, 4.5% at ten years, 5.5% at 15 years and 7% by age 25. The UK National General Practice Study of Epilepsy followed up children with febrile seizures for a mean of 21.6 years and found that 6% developed epilepsy over the whole follow-up period. The risk seemed to decrease with time[52].

Predisposing factors for later afebrile seizures

Family history of epilepsy. The information from population-based studies is conflicting. The NCPP[10] found that a history of seizures without fever in a parent or prior-born sibling was associated with a threefold increase in the rate of subsequent epilepsy after febrile convulsions. However Annegers et al[3] found only a weak association.

Age of onset of febrile convulsions. In the population-based NCPP[9] there was an increased rate of epilepsy by seven years of age in children whose febrile convulsions began in the first year and especially in the first six months. However there was a tendency for abnormal children to have convulsions early which might explain the increased risk of epilepsy in this group. Annegers et al[3] found that most of the increased rates associated with age were due to confounding by complex features of the febrile convulsions.

Abnormal neurological or developmental status. In the NCPP[9] children who had neurological or developmental abnormality before the first febrile convulsion were three times more likely to be epileptic by the age of seven years than those who were previously normal.

Characteristics of the febrile convulsions. Afebrile seizures occur with increased frequency after convulsions that are 'complicated' or 'complex'. In the American cohort study, the NCPP[9], the rate of spontaneous epilepsy, not preceded by febrile convulsions, was 5/1000; after 'pure' febrile convulsions epilepsy developed in 15/1000 while after complex febrile convulsions epilepsy developed in 41/1000. The outcome also varied according to the type of complex febrile convulsion – when the first convulsion had prolonged, multiple or focal features epilepsy developed in 31, 42 and 71/1000, respectively. The British CHES[14] found very similar results, as did Annegers et al[3] – who found that the risk of what they called 'unprovoked seizures' ranged from 2.4% among those who had simple febrile convulsions to 6–8% for those with a single complex feature, 17–22% with two complex features and 49% with all three complex features.

Recurrent episodes of febrile convulsions. There are reports that an increase in the number of febrile recurrences is associated with an increased risk of later epilepsy[19]. However neither the NCPP[9] nor the Rochester Study[3] found much evidence for this.

Type of afebrile seizure after febrile convulsions
As discussed above, some studies suggest that febrile convulsions can cause temporal lobe damage and lead to afebrile complex partial seizures. Annegers et al[3] did find that children with febrile convulsions had a higher risk of later partial rather than generalised afebrile ('unprovoked') seizures. The prognostic factors for partial and generalised seizures were

different. Febrile convulsions that were focal, repeated or prolonged were strongly associated with partial afebrile seizures, whereas only the number of febrile convulsions was significantly associated with generalised-onset seizures. Verity and Golding[14] also reported an association between the occurrence of focal febrile convulsions and later afebrile complex partial seizures.

However population-based studies have shown that the distribution of generalised and complex partial seizures in those that have had febrile convulsions was similar to that in the general population, i.e. there was no excess of complex partial seizures in the febrile convulsion group[2,14,53]. This suggests that febrile convulsions do not contribute appreciably to the occurrence of complex partial seizures.

Neurological impairment

No child in the population-based NCPP[9] developed persisting hemiplegia or other motor deficit during or immediately after an asymptomatic febrile convulsion[10]. In the CHES cohort 398 children had febrile convulsions. A total of 19 (4.8%) had lengthy febrile convulsions (>30 minutes): in this group there was no evidence of neurological sequelae in those who had been normal before the lengthy attacks, except for one atypical case – a child who became very hyperpyrexial after he was put into a hot bath during a convulsion[15].

Maytal and Shinnar[54], in their study of 'febrile status epilepticus' (febrile convulsions lasting longer than 30 minutes), reported that no child died or developed new neurological deficits following the episodes of status.

Intellectual outcome

Ellenberg and Nelson[8] identified 431 sibling pairs that were discordant for febrile convulsions in the population-based NCPP and found that at seven years of age children who were normal before any febrile convulsion did not differ in IQ from their normal seizure-free siblings. Neither recurrent seizures nor those lasting longer than 30 minutes were associated with IQ deficit. Population-based studies in Britain[13,16] also found little difference in intellectual outcome between children who had febrile convulsions and their peers, if the children with febrile convulsions had no other known neurological abnormality. However specific cognitive difficulties have been described – Martinos et al reported that recognition memory is impaired in children after prolonged febrile seizures. When followed up after about a year the children were still showing deficiencies in recognising a face after a five-minute delay; this was associated with relatively small hippocampal volumes in those children[56].

Behaviour

Immediate and short-term effects on behaviour have been reported up to 35% of children after febrile convulsions. In the CHES cohort a comprehensive assessment at ten years of age found that the behaviour of children with febrile convulsions differed very little from their peers[16].

Outcome after febrile convulsions – conclusions

Authors who report a poor outcome tend to have studied selected groups of children attending specialised hospitals or clinics. Sometimes they have included children who have suffered with convulsions that complicate meningitis or encephalitis. Some have included children that were known to be developmentally or neurologically abnormal before they had their first febrile convulsion. In contrast population-based studies that have looked at a less selected

group of children give a much more positive view. Such studies show that most children with febrile convulsions are normal individuals who have simple febrile convulsions, the majority of which do not recur. In such children there is little evidence of long-term effects on behaviour or intelligence and the increased risk of later epilepsy is slight. The minority of children have complex febrile convulsions and for most of them the outlook is good. However within this group there are a few children who are at particular risk of having later epilepsy, the risk being greatest for those who have febrile convulsions with focal features, which tend to be prolonged and to occur in the younger children.

A study in the United States of children with febrile status epilepticus (lasting 30 minutes or more) found evidence of acute hippocampal T2 hyperintensity on MRI scans in a proportion of those children, followed by the radiological appearance of hippocampal sclerosis after one year. Longer follow-up is needed to determine the relationship of these findings to temporal lobe epilepsy[50].

Clinical characteristics

Febrile convulsions are all either tonic-clonic or possibly hypotonic in type and are never myoclonic seizures, spasms or non-convulsive attacks. Most are brief and bilateral, but long-lasting and/or partial (unilateral) febrile convulsions do occur: 70–75% of these are the initial febrile convulsion experienced by the child[17].

Simple febrile convulsions are the commonest type of febrile convulsion. They are brief (<15 minutes) generalised seizures that do not occur more than once during a single febrile episode. Some just consist of staring, perhaps accompanied by stiffening of the limbs and they may not cause the parents great concern. Often they are much more dramatic. In the CHES birth cohort[14] about 40% were not considered sufficiently severe to necessitate admission. About two-thirds of the children suffered only one febrile convulsion ever.

Complex febrile convulsions may be more severe than simple febrile convulsions – in the CHES cohort 95 children (25% of the children with febrile convulsions) had complex convulsions and 78% of them were admitted to hospital – a higher proportion than was found in those with simple convulsions[14]. In these 95 children the complex features were as follows: 55 (58%) multiple, 32 (34%) prolonged and 17 (18%) focal (some had more than one complex feature). It is important to emphasise that the most severe attacks made up a very small proportion of all febrile convulsions.

Management

Introduction
Management of children with febrile convulsions remains controversial[17-19,57-9]. Groups of experts have published guidelines. These include the Consensus Development Panel which met at the National Institutes of Health in America in 1980[60], the 1991 Joint Working Group of the Research Unit of the Royal College of Physicians (RCP) and the British Paediatric Association (BPA)[61] and the American Academy of Pediatrics[62-3].

Initial assessment
First the convulsion should be stopped if it is continuing. Then the temperature should be measured to confirm that the child is febrile (the rectal temperature is more reliable than oral or axillary). It is important to determine whether or not the fever preceded the convulsion. The parents/carers may report a febrile illness and they may have measured the child's temperature before the seizure started. The history and the general physical examination may provide clues: there may be an exanthematous rash or evidence of an upper respiratory tract

infection. If the child presents in a convulsion the situation should be reassessed when it has stopped. Even when there is evidence of an infection outside the nervous system it may be important to exclude an intracranial infection by performing a lumbar puncture.

Admission to hospital

Febrile convulsions that last for more than a few minutes should be stopped and if the convulsion cannot be stopped the child should be admitted to hospital. If the convulsion has stopped it must then be decided whether or not to admit. According to the RCP/BPA Joint Working Group[61] the following factors would favour admission after a first convulsion:

- Complex convulsion
- Child aged less than 18 months
- Early review by a doctor at home not possible
- Home circumstances inadequate, or unusual parental anxiety, or parents' inability to cope.

Investigations

'No investigations are routinely necessary in all children after a febrile convulsion', according to the RCP/BPA Joint Working Group[61]. This statement seems to be representative of the views of most commentators. It may be appropriate to check the blood glucose concentration or the electrolytes in some children with continuing convulsions.

Lumbar puncture

This is still a controversial subject. Rosman[59] recommends an active approach – lumbar puncture for all children less than two years old with febrile convulsions – and he suggests the need for a second lumbar puncture in some children with suspected meningitis, quoting evidence from Lorber and Sunderland[64] who reported that the CSF is sometimes normal early in the course of meningitis, although their general advice was that 'lumbar puncture should not be carried out as a routine procedure'. Rutter and Smales[65] also reported that two children in their series developed meningitis within one or two days of a negative lumbar puncture, so false reassurance can be derived from a lumbar puncture. Clinical vigilance seems to be all-important.

The RCP/BPA Joint Working Group[61] recommended a lumbar puncture if:

- There are clinical signs of meningism
- After a complex convulsion
- If the child is unduly drowsy or irritable or systemically ill
- If the child is less than 18 months old (probably) and almost certainly if the child is aged less than 12 months.

The group considered that ideally a decision should be made by an experienced doctor. If the decision is taken not to perform a lumbar puncture it should be reviewed within a few hours. The risk of coning in a comatose child should be borne in mind and so should the fact that clinical signs of meningism are much less likely to be found in younger children.

Camfield and Camfield[57] recommend a lumbar puncture for the majority of children under one year of age with a first febrile seizure because at that age meningitis may be accompanied by very little nuchal rigidity or other findings of meningeal irritation. Lumbar puncture is indicated when there is the possibility of a partially treated meningitis in a child who has already been given antibiotics. The American Academy of Pediatrics reached similar conclusions[62]. In a retrospective cohort review Kimia et al found that the risk of bacterial meningitis presenting as first simple febrile seizures at ages 6–18 months was very low[66].

It may be decided that lumbar puncture is contraindicated in a febrile child who does not return to normal consciousness after a prolonged convulsion – there is a risk of coning if the intracranial pressure is raised. In a retrospective review of the progress of 445 children admitted to hospital with bacterial meningitis Rennick et al[67] concluded that lumbar puncture may cause cerebral herniation in some cases, and normal results on computed tomography do not mean that it is safe to perform a lumbar puncture in a child with bacterial meningitis. It may be appropriate to start adequate doses of broad-spectrum antibiotics and delay the lumbar puncture.

EEG
Reviewers have concluded that EEGs are not helpful in assessing the prognosis of children who have febrile convulsions[17,19,57,68]. The EEG is therefore not recommended as part of the assesssment of a child with febrile convulsions.

Brain imaging
A child with a preceding or underlying neurological problem may first come to medical attention because of a febrile convulsion. Underlying pathology may therefore be suspected on the basis of the history or examination and it may then be appropriate to perform a scan to investigate. This situation will exist in only a small minority of children with febrile convulsions.

Acute therapy

Management of fever
Fever should be treated for the comfort of the child. Kinmonth et al[69] found that advice to give paracetamol was more effective than sponging or unwrapping in controlling temperature in children at home and was more acceptable to parents. The RCP/BPA Joint Working Group did not recommend physical methods such as fanning, cold bathing and tepid sponging[61].

Rectal diazepam to abort febrile convulsions
The home use of rectal diazepam to abort seizures in children with convulsive disorders has been shown to be effective[70-72]. Some members of the RCP/BPA Joint Working Group (1991) advised parents to give the drug as soon as possible, some advised that the parents wait for five minutes, by which time most convulsions will have stopped and the drug will be unnecessary. There is now evidence that buccal midazolam is as safe and effective in controlling febrile seizures as rectal diazepam[73].

Prophylactic treatment

Intermittent prophylaxis
One approach to preventing recurrent febrile convulsions is to intervene at the onset of febrile illnesses in the child at risk. Active steps to lower the body temperature have been advocated and so has the prophylactic use of diazepam.

Antipyretic measures. Camfield et al[74] studied antipyretic instruction plus either phenobarbitone or placebo to prevent recurrence after the first febrile seizure. Despite verbal and written instructions about temperature control and demonstration of the use of the thermometer, there was little evidence that antipyretic counselling decreased seizure recurrence amongst patients receiving placebo. The MRC/BPA working group met in 1990 and at that time the members knew of no evidence that antipyretic treatment influenced the recurrence of febrile seizures[61]. In an editorial Camfield et al[75] concluded that there was no evidence that the usual methods of fever control have any effect on recurrences of febrile seizures. In their opinion the continuing recommendation that parents document fever and

use antipyretic agents was likely to (inappropriately) increase parental anxiety and 'fever phobia'.

Intermittent prophylactic anticonvulsants. Intermittent prophylactic oral or rectal diazepam reduce the number of febrile recurrences. The guidelines published by the MRC/BPA Joint Working Group[61] acknowledged that rectal diazepam could be effective in preventing convulsions when given at the onset of fever and a large oral dose of phenobarbitone may give an effective blood concentration in 90 minutes, but did not recommend the use of either drug in this way because both caused drowsiness.

Since then a randomised placebo-controlled trial in America concluded that oral diazepam, given only when fever is present, is safe and reduces the risk of recurrent febrile seizures[76]. On the basis of the results the authors recommended starting oral diazepam at the first sign of illness. Treatment with diazepam should then continue if the child becomes febrile, and should stop after a day or two if no fever develops. In the paper the authors stated that diazepam has no serious side effects, but 38.6% of the 153 children who received at least one dose of diazepam had what the authors termed moderate side effects. These included ataxia (30.0%), lethargy (28.8%) and irritability (24.2%).

In their editorial review Camfield et al[75] pointed out that the only placebo-controlled trials of intermittent administration have been with orally administered diazepam. A meticulous study by Uhari[77] had shown no benefit in preventing recurrence, even when the oral diazepam was combined with acetaminophen. Autret et al[78] also found no benefit from diazepam – the authors concluded that the failure was due to the difficulties of early identification of the fever and the logistics of administering medication intermittently to children with multiple carers rather than to the ineffectiveness of the drug.

Continuous prophylactic anticonvulsants

'The vogue for long-term anticonvulsant prophylaxis against febrile convulsions seen in the 1970s and early 1980s has passed', according to the RCP/BPA Joint Working Group[61].

What is the basis for making the decision about giving medication to prevent recurrences? Aicardi[17] reviewed the research into the continuous oral use of drugs to prevent recurrence of febrile convulsions. This can be summarised as follows:

- Phenobarbitone at a dose of 4–5 mg/kg/day reduces the number of febrile recurrences; phenobarbitone has a number of behavioural side effects, intolerable behaviour being reported in up to 21% of children taking the drug.
- Sodium valproate has also been shown to prevent febrile recurrences.
- Experience with other continuous anticonvulsants is limited and unsatisfactory.

Despite the evidence that drugs can reduce recurrences there are good arguments that prophylactic medication is rarely indicated. In the American NCPP cohort[9,10] there were 1706 children with febrile convulsions who were assessed at seven years of age. Not one child had a brief initial febrile convulsion that was followed by a prolonged recurrence and then by epilepsy. This undermines the argument that prevention of febrile recurrences will prevent 'brain damage' and thus reduce the risk of developing epilepsy.

In the NCPP 90% of the children who were epileptic after febrile convulsions by seven years had never had a febrile convulsion that lasted as long as 30 minutes. In the minority who became epileptic after having had a lengthy seizure, this was the first seizure of their lives. Similar conclusions have been reached as a result of the more recent population-based CHES[14].

There is particular concern that prolonged febrile convulsions cause mesial temporal sclerosis. The data provided by the CHES cohort led to the following conclusions:

- If prolonged febrile convulsions actually cause temporal lobe damage (rather than being the first overt evidence of such damage) it happens relatively rarely (three children out of 392 with febrile convulsions in the cohort).
- If damage does occur it is likely to have happened by the time that the child first gets to a doctor (most children with complex febrile convulsions have them as the first attack).
- Recommendations that have been made about the use of prophylactic anticonvulsants in children with febrile convulsions have been unduly influenced by the anxiety about this very small group of children.

Studies have cast doubt on the effectiveness of anticonvulsants in preventing recurrences of febrile seizures. A British study of the use of sodium valproate and phenobarbitone in preventing recurrence of febrile convulsions was analysed on an intention-to-treat basis. The overall risk of recurrrence was 30% and prophylactic treatment did not lessen this risk[79]. Newton[80] pooled the results from six British trials of phenobarbitone and four of valproate and analysed them on an intention-to-treat basis, showing little overall value in treating children who have febrile convulsions with anticonvulsants. Farwell et al[81] studied the use of phenobarbitone in children who had had at least one febrile convulsion and were at heightened risk of further convulsions. The results showed that phenobarbitone depressed cognitive performance in children treated for febrile convulsions and that this may outlast the administration of the drug by several months. There was no reduction in the rate of recurrence of febrile convulsions in the phenobarbitone group compared to the placebo group.

A Cochrane Database systematic review by Offringa and Newton concluded that no clinically important benefits for children with febrile seizures were found for intermittent oral diazepam, phenytoin, phenobarbitone, intermittent rectal diazepam, valproate, pyridoxine, intermittent phenobarbitone, or intermittent ibuprofen, nor for diclofenac versus placebo followed by ibuprofen, acetaminophen or placebo. Adverse effects of drugs were reported in up to 30% of children. They concluded that parents should be supported with practical advice and reassured about the benign nature of recurrent febrile seizures[82].

Summary

General outcome
Febrile convulsions are common. The majority are simple febrile convulsions – brief generalised seizures that occur just once in the lifetime of normal children. The evidence is that most children who have febrile convulsions of any type (simple or complex) are subsequently normal in intellect, neurological function and behaviour.

Subsequent epilepsy
For most children with febrile convulsions the risk of later epilepsy is little different from that in the general population. A minority of children who have febrile convulsions are at increased risk of developing epilepsy – those that are neurologically or developmentally abnormal before the convulsions and some of those who have febrile convulsions with complex features, particularly if focal.

Initial management
Most febrile convulsions stop spontaneously and not all children need to be admitted to hospital. It is reassuring if the child seems neurologically normal after the convulsion. However, prolonged seizures should be stopped by appropriate acute treatment and if there

is any other concern about the child's neurological state hospital assessment is appropriate. A lumbar puncture may be necessary to exclude meningitis in the minority of cases, particularly in children younger than 18 months. Ideally this decision should be made by an experienced doctor. Investigations are not routinely indicated after febrile convulsions – the EEG is not helpful and brain scans are rarely indicated.

Subsequent medication

If febrile convulsions are prolonged it may be appropriate to teach parents to administer buccal midazolam or rectal diazepam at home to prevent further prolonged episodes. There is no convincing evidence that antipyretic measures reduce the frequency of febrile recurrences or that the administration of intermittent or continuous prophylactic anticonvulsant medication reduces the risk of later epilepsy. Prophylactic medication is now not generally advised for children with febrile convulsions.

Information for carers

Many parents/carers are very distressed when they witness febrile convulsions in their children and it should be a priority to inform them about the essentially benign nature of most febrile convulsions. When assessing the prognosis it is relevant to consider the type of febrile convulsion and the clinical context in which it occurs, but parents can be reassured that for the majority of children with febrile convulsions the outcome is good and that medication is rarely indicated. Ideally, written information should supplement the interview and there are now excellent videos that provide advice and support for parents.

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