Febrile Seizures: Current Concepts Concerning Prognosis and Clinical Management

Mary Sollinger Applegate, MD, and Warren Lo, MD
Columbus, Ohio

Febrile seizures are a common problem in young children. Most febrile seizures are benign in nature, although a small percentage of children may develop recurring febrile seizures or afebrile seizures. The approach to the management of this disorder varies widely from specialty to specialty despite the recent publication of studies that provide for rational treatment of febrile seizures. Most children do not need any treatment after a first simple febrile seizure. In certain children who are at risk for recurrent febrile seizures, rectal anticonvulsants should be considered for acute, short-term management. Long-term anticonvulsants should be reserved for patients who are unable to use rectal anticonvulsants or who have significant risk factors for the development of afebrile seizures.

Febrile seizures affect between 2% and 5% of all children, account for 2.1% of all pediatric clinic or hospital visits, and account for 30% of all childhood seizures.[1,2] In the United States, febrile seizures affect 3% to 4% of all children before the age of 5 years, roughly one-half million children per year.[3–6] Febrile seizures usually occur as a single, isolated episode in most children. A proportion of children will develop recurring febrile seizures; however, a smaller proportion will develop recurring afebrile seizures (ie, epilepsy). The management of febrile seizures can be perplexing, since these seizures are benign in most children. The reported development of sequelae has varied from zero to 100% in earlier studies because of inconsistencies in the definition of febrile seizures, methods of case selection, number of patients under study, duration of follow-up, and location of the investigation. More recent studies of febrile seizures have provided a better picture of the clinical course of this disorder and have better defined the risk factors for sequelae. A rational approach to the management of febrile seizures depends upon one's understanding of the results of these studies. First, the important features of febrile seizures will be reviewed. Second, the recent studies identifying risk factors for the development of sequelae will be reviewed. Third, the management of febrile seizures will be discussed.

Submitted, revised, August 2, 1989.

From the Department of Pediatrics, Ohio State University College of Medicine, Columbus, Ohio. Requests for reprints should be addressed to Dr Warren Lo, B-403 Children's Hospital, 700 Children's Drive, Columbus, OH 43205.

USUAL FEATURES OF FEBRILE SEIZURES

Febrile seizures are brief, generalized, clonic, or tonic-clonic attacks with little postictal confusion or weakness. Most children develop a temperature of 39 °C (102.2 °F) or greater at the time of the seizure, although the temperature can range from 38 °C to 41 °C.[1,2] Febrile seizures usually occur between the ages of 3 months and 7 years; 95% occur before the age of 5 years. Both sexes have a peak incidence of febrile seizures at 23.2 months.[7] The definition of febrile seizures excludes (1) seizures caused by central nervous system infections, (2) underlying afebrile seizure disorders in which the fever precipitates a seizure, and (3) recurring afebrile seizures, ie, epilepsy.[3,8,9]

Febrile seizures occur frequently in shigellosis, salmonellosis, and roseola infantum.[10–12] Otherwise, no study has shown a causal relationship between febrile seizures and any other specific type of infection or infectious agent. The general belief is that the fever resulting from an infection is the most important factor in the cause of febrile seizures rather than the nature of the infection or the causative organism. Febrile seizures do not always occur at the height of the fever; they may occur at the onset of the febrile illness. Some authors postulate that the rapid rise in temperature may lower a critical threshold in susceptible

TABLE 1. SIMPLE VS COMPLEX FEBRILE SEIZURES[5,7]

Characteristics	Simple Seizure	Complex Seizure*
Type of seizure	Generalized	Focal
Duration	Less than or equal to 15 min	Longer than 15 min
Frequency	Once per 24-h period	More than once per 24-h period

Any one of the listed features make the seizure complex

children, and that the rate of rise in temperature is more important than the absolute temperature in the production of the seizure.[9,13]

SEQUELAE OF FEBRILE SEIZURES

The most important sequelae of febrile seizures are recurrent febrile seizures and epilepsy. To understand who is at risk for developing these sequelae, one must distinguish simple from complex febrile seizures (Table 1).[5,7,9] A simple febrile seizure is generalized, lasts less than 15 minutes, and occurs no more than once within a 24-hour period. Characteristics that distinguish a complex febrile seizure are that it may be focal, may last more than 15 minutes, or may occur more than once in a 24-hour period. Only 16% to 18% of all febrile seizures are classified as complex.[3,7]

American studies of the sequelae of febrile seizures were performed by Nelson and Ellenberg,[3,7] who used the data of the National Collaborative Perinatal Project (NCPP), and Annegers and co-workers,[14] who looked at 687 children in the Rochester Epidemiology Project. British studies were performed by Verity and co-workers,[15] who studied 303 children with febrile seizures identified in the British Child Health and Education Study, and Ross and co-workers,[16] who reported on 1043 British children who had a history of seizures by 11 years of age.

The simple febrile seizure has a lower risk for sequelae than a complex seizure. Nelson and Ellenberg found that of children who had one simple febrile seizure, 65% had no further seizures by the age of 7 years, 32% had more than one febrile but no afebrile seizures, 3% had at least one afebrile seizure, and 2% developed epilepsy (recurring afebrile seizures).

In the NCPP study, patients with simple febrile seizures had a fourfold greater rate of developing epilepsy by the age of 7 years compared with the 0.5% incidence of epilepsy in the general population. Ross and co-workers[16] in the British National Child Development Study found that only 0.1% of patients with febrile seizures developed epilepsy. Annegers et al[14] found slightly different results in a more recent study of 687 children with febrile seizures. They determined that the risk for epilepsy escalates with increasing age and length of follow-up. Annegers et al reported that patients with simple febrile seizures had a 7% risk of developing afebrile seizures by the age of 25 years, a fivefold greater risk than in the general population. Despite the slight discrepancies between these studies, the findings of Nelson and Ellenberg, Ross and co-workers, and Annegers and co-workers indicate that the risk of epilepsy, while higher than in the general population, was still quite low in patients with simple febrile seizures.

Recurrent Febrile Seizures

Recurrent febrile seizures are the most common sequelae of febrile seizures. Of the 1706 children followed in the NCPP study, 33% had at least one recurrence, 17% of the total had a second recurrence, and 9% of the total had three or more recurrences.[3] Fifty percent of the recurrences happened within 6 months and 95% within the first year of the first febrile seizure. The recurrences showed no preference for either sex, and were not affected by whether the first seizure was complex. If the first febrile seizure occurred within the first year of life, recurrences were more common.[17] Similar results were obtained in the British Child Health and Education study.[15] In that study, 65% had only one febrile seizure, 35% had at least one recurrence, 9% had two recurrences, and 13% had three or more recurrences.

The two factors that identified an increased risk for recurrent febrile seizures were age less than 1 year at the time of the first febrile seizure and a positive family history for febrile seizures.[3,16]

The chance of developing a complex febrile seizure after a simple febrile seizure was 8% and remained 8% for each subsequent seizure.[3]

Epilepsy

The risk factors for the development of epilepsy are complex febrile seizures, abnormal neurologic function, multiple febrile seizures, and a family history of epilepsy. Nelson and Ellenberg,[7] Annegers and co-workers,[5] and Ross and co-workers[16] found no association between the development of epilepsy and age, sex, Apgar scores, birthweight, brain malformations, or electroencephalogram changes.

Complex Febrile Seizures

A complex febrile seizure is one risk factor for the development of epilepsy. In the NCPP, children who had a complex febrile seizure developed epilepsy at a rate of 41 per 1000. In contrast, children with a first simple febrile sei-

TABLE 2. CUMULATIVE RISK (IN PERCENT) FOR DEVELOPING UNPROVOKED SEIZURES* AFTER A FEBRILE SEIZURE

Number of Complex Features Present During Initial Seizure	Risk of Unprovoked Seizures
0	2.4
1	6–8
2	17–22
3	49

*Until age 25 years
Data taken from Annegers, et al[14]

zure developed epilepsy at a rate of 15 per 1000.[7] Children in the general population developed epilepsy at a rate of only 5 per 1000. These results were the same regardless of whether the complex febrile seizure was a first or a subsequent seizure. Annegers and co-workers[14] found that each of the three complex features was an independent, although interrelated, risk factor for the development of afebrile seizures. Furthermore, they found that the number of complex features occurring during the febrile seizure increased the risk for developing unprovoked seizures (Table 2). One may summarize these studies by stating that a febrile seizure with one or more complex features increased the risk of developing epilepsy.

Neurological Status

An abnormal neurological status prior to the occurrence of a febrile seizure was a major risk factor for the development of epilepsy.[5,7] Twenty-two percent of the 1706 children in the NCPP study had a neurological deficit or developmental delay before their first febrile seizure. In that study, children with a neurological abnormality before their first febrile seizure had a fivefold greater risk of developing epilepsy than normal children. Children with both an abnormal neurological examination and a complex febrile seizure had an 18-fold greater risk of developing epilepsy than the general population.

Number of Febrile Seizures

Nelson and Ellenberg[7] observed that the total number of febrile seizures did not affect the risk of epilepsy if the child had a normal neurological examination, but the risk increased markedly in children with abnormal examinations and three or more febrile seizures. Annegers and co-workers[14] found that having three or more febrile seizures increased the risk for the development of epilepsy, regardless of neurological abnormalities. They found a 4% risk of developing unprovoked seizures when three or more seizures were analyzed as the sole risk factor.

Age

The NCPP study found that the child's age when the first febrile seizure occurred was a significant risk factor for the development of epilepsy if the seizure occurred within the first year of life.[7] Children whose first febrile seizure occurred during the first 6 months of life had a 5.7% risk of developing epilepsy compared with a 1.5% risk for children whose first febrile seizure occurred between the 6th and 12th month of life. If the first seizure occurred after age 1 year, there was no increased risk for the development of epilepsy. Other investigators[4,5,8] also found that the onset of febrile seizures at an early age was a risk factor for epilepsy. In contrast, Annegers and co-workers[14] found that an age of less than 1 year was not a significant risk factor when the effects of other risk factors were removed.

Family History

An important risk factor is a history of afebrile seizures in the immediate family. In the NCPP this factor was associated with a 1.6- to 3-fold increase in the risk of developing epilepsy.[7,14] A family history of febrile seizures bore no significance, although some studies dispute this observation.[5,18,19]

SUMMARY OF RISK FACTORS FOR THE DEVELOPMENT OF EPILEPSY

The following characteristics are risk factors for the future development of epilepsy in children with febrile seizures:

1. Febrile seizures with any complex features
2. An abnormal preseizure neurological status
3. A history of three or more febrile seizures
4. Positive family history for afebrile seizures

As might be expected, the more risk factors present, the greater the risk of developing epilepsy or unprovoked seizures.[3,14] Nelson and Ellenberg[3] stated that two or more risk factors were associated with a 10% chance of developing epilepsy.

Annegers and co-workers[14] further evaluated the risk factors and their association with partial seizures. They determined that a complex feature of a seizure was associated with the development of an unprovoked partial seizure. They found that a small number of febrile seizures (three or fewer) and a positive family history of seizures were more closely associated with developing an unprovoked generalized seizure than with developing a partial seizure.

OTHER SEQUELAE

Deaths or Motor Deficits

In the NCPP study, no deaths or persisting motor deficits occurred among patients with febrile seizures.[3] There was a 0.4% incidence of a Todd's paresis (postictal weakness) lasting 7 days or less. Older studies have reported occasional hemiplegia, choreoathetosis, and decorticate rigidity, but these sequelae are very rare.[20,21]

Intelligence

Most studies agree that febrile seizures do not cause either intellectual deterioration or learning disabilities.[15,16,22] Ellenberg and Nelson[22] studied 431 sibling pairs in which only one sibling experienced a febrile seizure. They found that at age 7 years there was no lower intelligence quotient or drop in academic performance in the sibling with febrile seizures. The only children with intelligence quotients significantly lower than their seizure-free siblings were (1) children who had an abnormal preseizure neurological or developmental status, and (2) children who subsequently developed afebrile seizures, especially minor motor seizures.

Whether a severe febrile seizure can cause mental retardation is still being debated. Some authors[23] have associated long, complicated febrile seizures with the development of mental retardation and neurologic sequelae; however, the NCPP investigation[22] and the British Child Health and Education Study[15] found no correlation between the duration, severity, or number of febrile seizures and mental retardation.

DIFFERENTIAL DIAGNOSIS

One of the major concerns in the case of a young child presenting with fever and seizures is the possibility that the child actually has meningitis. Thirteen percent to 18% of children with meningitis have seizures as a presenting sign. Children under 2 years of age may not have nuchal rigidity, and meningitis may be difficult to diagnose in children younger than 2 to 3 months.[24] In a young child, especially under the age of 6 months, presenting with fever and a first seizure, one must consider meningitis in the differential diagnosis. In addition, less common causes of seizures should be considered such as acute encephalopathies of metabolic or toxic origin, hypoglycemia, anoxia, trauma, tumor, and hemorrhage. Entities that may be confused with febrile seizures include febrile delirium and febrile shivering accompanied by general pallor and perioral cyanosis. A careful review of the history and a thorough physical examination are essential for making an accurate diagnosis, since the patient is often seen by the physician after the seizure has ceased.

TREATMENT

The initial management of a febrile seizure is dictated by the clinical setting. If the seizure has ended and the patient is awakening, the patient may be carefully examined for a source of the fever as the history is obtained. Intravenous anticonvulsants need not be given at this stage, since most febrile seizures will not recur, and even if another seizure occurs, it usually will stop spontaneously in less than 5 to 10 minutes. If the patient is still having a seizure, the adequacy of the airway, breathing, and circulation should be determined and protected. The patient should be placed in the lateral decubitus position to minimize the risk of aspiration and airway occlusion.

There is no definite evidence that a reduction in body temperature will stop a seizure or prevent a rapid recurrence; however, fever is usually treated with a tepid sponge bath and oral or rectal acetaminophen (10 mg/kg). Aspirin has been used in the past, but concerns recently have arisen regarding the association between aspirin use and Reyes' syndrome.[25]

If a febrile seizure lasts more than 10 minutes, medication to stop the seizure is indicated. Intravenous diazepam or lorazepam (0.1 to 0.2 mg/kg to a maximum initial dose of 10 mg)[26,27] are fast, short-acting benzodiazepines that are common first-line agents. Since they can cause cardiorespiratory depression, one must be prepared to protect the airway and maintain ventilation when using these drugs intravenously. These medications should not be injected intramuscularly because they do not achieve effective blood levels.[6,26,27] A growing number of authors[28–31] have proposed that diazepam be given rectally either by suppository (not available in the United States) or by giving the injectable solution as an enema to stop prolonged febrile seizures, especially when intravenous access is difficult to establish.

Intravenous phenytoin or phenobarbital at a dose of 10 to 15 mg/kg may be used to stop prolonged seizures, but these drugs pose certain inconveniences. Both have an onset of action lasting in the range of minutes, and furthermore, phenobarbital may cause respiratory depression, phenytoin may cause cardiac arrhythmias, and both drugs can cause hypotension.[6,26,27] Whenever phenytoin or phenobarbital are given intravenously, the patient's respiration, pulse, and blood pressure should be carefully monitored. If one cannot get intravenous access and a long-acting drug is desired, valproic acid is another anticonvulsant that can be administered rectally to control prolonged seizures in the acute setting. The usual starting dose is 40 to 60 mg/kg diluted in an equal volume of tap water, given as a retention enema. The onset of duration for valproic acid is also in the range of minutes. This drug should be used with caution in very young children because of the slight risk of fatal hepatotoxicity.[32]

Occasionally, a patient will have more than one febrile seizure in a 24-hour interval. A second, single febrile seizure does not mandate treatment; however, if the patient has multiple seizures within a day, the patient should probably be treated with an oral anticonvulsant, at least temporarily, to suppress seizure recurrence.

Once the seizure has stopped, the child should be examined so that the cause of the fever and any neurological deficits can be identified. Treatable causes of a seizure, such as an acute infection, hypoglycemia, or electrolyte disturbance, should be ruled out, particularly if the patient is less than 1 year of age.

A frequent question that arises with a first febrile seizure is whether to examine the cerebrospinal fluid. Since the consequences of an undiagnosed meningitis are so grave, a lumbar puncture should, in general, be performed in children under the age of 1 year who have experienced their first febrile seizure.[27] If the patient has had a simple febrile seizure, has a detectable source for the fever, is recovering and appears well, then additional diagnostic studies, such as an electroencephalogram or a computed tomographic brain scan, are usually unnecessary. If the child has had a focal seizure or focal neurological abnormalities, a computed tomographic brain scan may help detect any unsuspected structural lesions.

If the patient has had a simple recurrent febrile seizure and the physical examination is normal, an extensive reevaluation is not needed. Computed tomographic brain scans, blood glucose levels, calcium and magnesium levels, or electroencephalograms are unnecessary in this setting. Some physicians perform lumbar punctures on children younger than 1 year of age even with recurrent febrile seizures[24,33]; however, if the child has had a previous febrile seizure(s), if the child is older than 6 months, and if there is little clinical suspicion of meningitis or encephalitis, then a lumbar puncture is probably unnecessary.

LONG-TERM CARE

After the acute febrile seizure has ceased, the next questions are whether and how to prevent recurrent seizures.

Recurrent Febrile Seizures

Some physicians argue that recurrent febrile seizures should be prevented, since they are frightening and generate panic and anxiety among parents.[34] One must consider, however, whether prophylaxis against recurrences is necessary in the vast number of children with febrile seizures. If a child has had only one febrile seizure, then the need for prevention has not been definitely established since two thirds of children with a first febrile seizure will have no recurrence. In this instance, treatment will be simpler if medication can be avoided. If the child has risk factors for recurring febrile seizures (age of onset less than 18 months and a family history of febrile seizures), or if the child has had three or more febrile seizures (thereby establishing a pattern of recurrence), then prophylactic treatment is reasonable.

Intermittent Prophylaxis

Intermittent prophylaxis of febrile seizures is less complicated than continuous therapy because exposure to drug side effects is minimized, and the problems of compliance are avoided. Some physicians contend that recurrent febrile seizures can be prevented by reducing the fever with an antipyretic or by giving several doses of an oral anticonvulsant such as phenobarbital when the child develops a fever. These types of intermittent prophylaxis are ineffective because (1) 30% of the caretakers are unaware of a child's fever before the seizure, and (2) 80% of the fevers begin less than 24 hours before the seizure. Therapeutic serum phenobarbital levels cannot be obtained in such a short time without encountering substantial toxicity.[35]

Ideally, intermittent prophylaxis will employ a readily administered, short-acting anticonvulsant that is rapidly effective during the febrile illness and that can be stopped when the illness has resolved. Diazepam, administered rectally, is one type of intermittent therapy that is increasingly used. After initial reports from Europe,[29,30] rectally administered diazepam has achieved growing acceptance both as a prophylactic drug against febrile seizures and as an immediate treatment for prolonged febrile seizures. Knudsen[30] proposed that when a child with known recurrent febrile seizures develops a fever greater than 38.5 °C, the child should be given rectal diazepam every 12 hours until the fever ceases. The dose Knudsen used in the study was 5 mg for children younger than 3 years of age, and 7.5 mg for children aged between 3 and 6 years. An alternative regimen was used by Lee and colleagues,[29] who gave rectal diazepam as a suppository at a dose of 0.5 mg/kg every 8 hours when the temperature was equal to or greater than 38.5 °C for a maximum of 40 hours. The results of a US study of the use of oral diazepam as intermittent prophylaxis have not yet been published.[31]

Continuous Prophylaxis

If intermittent therapy proves unworkable (because of poor compliance, difficulty recognizing the onset of fever, or intolerance of the intermittent medication) and if continuous prophylaxis is justifiable, then the next choice for the prevention of recurrent febrile seizures is to prescribe

daily medication for the time that the patient is at risk for seizures. The two choices are phenobarbital and, with appropriate caution, valproic acid. Phenobarbital, at daily doses of 3 to 5 mg/kg, has been used most frequently in the United States. Studies have shown a seizure recurrence rate of 4% to 13% in patients treated with phenobarbital compared with a recurrence rate of 33% in untreated children in the National Collaborative Perinatal Project study.[35,36] The long-term use of phenobarbital, however, is fraught with problems of poor compliance and side effects. In Wolf and Forsythe's study,[37] 42% of 109 children treated with daily phenobarbital developed behavior disorders, mostly hyperactivity. Therapy was discontinued in one half of the children. For these reasons, Vining and Freeman[9] discourage routine prophylaxis for children with simple febrile seizures.

The alternative to phenobarbital is valproic acid. Valproic acid effectively prevents recurrent febrile seizures,[29] and the incidence of sedation and behavioral changes is lower with valproic acid than with phenobarbital. Rare cases of idiopathic, fatal hepatotoxicity have occurred with valproic acid, however.[32] Unfortunately, the rate for the development of this complication is highest in children under 2 years of age, the population that tends to have a high incidence of febrile seizures. The risk for developing hepatotoxicity is lower in children older than 2 years of age. Phenytoin and carbamazepine have been shown to be ineffective for prophylaxis of febrile seizures.[38,39]

There are no standard recommendations for the duration of continuous prophylaxis. Most recurrent febrile seizures occur within the year following the febrile seizure; therefore, it seems reasonable to continue therapy for 1 year after the last febrile seizure. Since the frequency of recurrences varies inversely with age, but the period of risk can extend to age 7 years, some physicians continue therapy either until the child reaches the age of 3 years, or until 1 year after the last seizure, whichever is longer.[1]

Prevention of Epilepsy

The choices between intermittent and continuous therapy and the duration of therapy are the same if one wishes to treat for the prevention of epilepsy as in the prevention of recurrent febrile seizures. Whether prophylaxis actually prevents epilepsy is a more complicated issue. Some authors have proposed that the prevention of recurring febrile seizures will prevent the development of mesial temporal lobe sclerosis, and thus prevent the development of epilepsy. Studies of patients undergoing temporal lobectomy for seizure control identified a history of febrile seizures in a higher proportion of the patients than in the normal population.[40] Since several of the excised temporal lobes had sclerosis of the medial temporal lobe, the concern was raised that recurring febrile seizures may lead to the development of mesial temporal lobe sclerosis, and that the sclerosis subsequently leads to the development of epilepsy. Those studies, however, examined a highly selected group of patients whose seizures were uncontrolled by standard medical therapy. Whether the association is causal or happenstance is still open to question.[41]

Given the above uncertainty about the cause-and-effect relationship between febrile seizures and epilepsy, it is difficult to provide clear-cut guidelines. Currently many physicians treat children at substantial risk for the development of epilepsy with continuous prophylaxis, although there is no hard evidence that continuous prophylaxis will actually prevent epilepsy.[42] Because debate exists over what constitutes sufficient risk to justify subjecting the patient to daily treatment, Nelson and Ellenberg[7] proposed that two or more of the following risk factors are sufficient: (1) a complex febrile seizure, (2) an abnormal preseizure neurological examination, and (3) a positive family history of afebrile seizures. Annegers et al[14] suggested that the presence of two or more of the complex features constitute a similar risk. In some cases, parental anxiety or inaccessible health care may prompt continuous prophylaxis.

CONCLUSIONS

Febrile seizures affect a large number of children, but most children do not develop any sequelae. There is no evidence that febrile seizures cause intellectual impairment or physical handicap, and there is no conclusive evidence that febrile seizures by themselves cause epilepsy. A child's having a febrile seizure appears not to cause any harm, but many physicians try to prevent recurrent febrile seizures to reduce the risk of physical injury during the seizure and to reduce parental anxiety. Based upon the results of recent studies, it is now possible to identify groups of children who are at increased risk for the development of recurrent febrile seizures. Children who have either a family history of febrile seizures or the onset of febrile seizures at 18 months of age or earlier have a greater risk for developing recurrent febrile seizures than the general population. These children, especially those with actual recurrences, should be considered candidates for either intermittent or continuous prophylaxis.

Whether one should treat febrile seizures in an attempt to prevent epilepsy is an individual decision. Children who develop epilepsy comprise somewhere between 2% and 7% of all children who have had febrile seizures. Whether treatment actually reduces the incidence of epilepsy is unknown, and it is unlikely that a randomized, controlled study will ever be carried out to test this question. If one decides to treat, the populations to consider treating are patients with a combination of the following: preexisting neurological abnormalities, two or more complex features,

multiple febrile seizures, and a strong family history of epilepsy.

A thoughtful, patient, and sensitive explanation of febrile seizures to the family is an important aspect of treatment. Educating the family to the generally good prognosis of febrile seizures, the absence of any impact upon mental and physical well-being, and the uncertainty of any causal link between febrile seizures and epilepsy will often allay the family's fears. If parents understand the benefits and risks of treatment and the reasons for not treating the patient, they can work together with the physician in developing a rational approach to therapy.

Acknowledgment

Dr. Warren Lo was supported in part by a grant from the National Institutes of Health, No. 1-K08-NS01235-01A1.

References

1. Aicardi J: Epilepsy in Children. New York, Raven Press, 1986, pp 212–232
2. Gururaj VJ: Febrile seizures. Clin Pediatr 1980; 19:731–738
3. Nelson KB, Ellenberg JH: Prognosis in children with febrile seizures. Pediatrics 1978; 61:720–727
4. Freeman JM: Febrile seizures: A consensus of their significance, evaluation, and treatment. Pediatrics 1980; 66:1010
5. Annegers JF, Hauser WA, Elveback LR, Kurland LT: The risk of epilepsy following febrile convulsions. Neurology 1979; 29:297–303
6. Camfield PR, Camfield CS: Toward a standardized approach to febrile seizures. ER Rep 1981; 2:18
7. Nelson KB, Ellenberg JH: Predictors of epilepsy in children who have experienced febrile seizures. N Engl J Med 1976; 295:1029–1033
8. Consensus development conference on febrile seizures. Proceedings. Epilepsia 1981; 22:377–381
9. Vining EPG, Freeman JM: Seizures which are not epilepsy. Pediatr Ann 1985; 14:711–723
10. Lahat E, Aladjem M, Heipert J, Mundel G: Shigellosis: Incidence of convulsions and resistance to antibiotics. Helv Paediatr Acta 1984; 39:123–128
11. Fischler E: Convulsions as a complication of shigellosis in children. Helv Paediatr Acta 1962; 17:389–394
12. Lennox-Buchtal MA: Neutropenia in children with febrile convulsions: Clinical correlations. Dev Med Child Neurol 1972; 14:21–30
13. Millichap JG: Febrile Convulsions. New York, Macmillan, 1968
14. Annegers JF, Hauser WA, Shirts SB, et al: Factors prognostic of unprovoked seizures after febrile convulsions. N Engl J Med 1987; 316:493–498
15. Verity CM, Butler NR, Golding J: Febrile convulsions in a national cohort followed from birth. II: Medical history and intellectual ability at 5 years of age. Br Med J 1985; 290:1311–1315
16. Ross EM, Peckham CS, West PB, Butler NR: Epilepsy in childhood: Findings from the National Child Development Study. Br Med J 1980; 280:207–210
17. Nelson KB, Ellenberg JH: Febrile seizures. In Dreifuss F (ed): Pediatric Epileptology. Boston, John Wright, 1983, pp 173–198
18. Hauser WA, Annegers JF, Anderson E, et al: The risk of seizure disorders among relatives of children with febrile convulsions. Neurology 1985; 35:1268–1273
19. Frantzen E, Lennox-Buchtal MA, Nygaard A, et al: A genetic study of febrile convulsions. Neurology 1970; 20:909–917
20. Aicardi J, Chevrie JJ: Febrile convulsions: Neurological sequelae and mental retardation. In Brazier MAB, Coceani F (eds): Brain Dysfunction in Infantile Febrile Convulsions. New York, Raven Press, 1976, pp 247–257
21. Wallace SJ: Neurological and intellectual deficits: Convulsions with fever viewed as acute indications of life-long developmental deficits. In Brazier MAB, Coceani F (eds): Brain Dysfunction in Infantile Febrile Convulsions. New York, Raven Press, 1976, pp 259–277
22. Ellenberg JH, Nelson KB: Febrile seizures and later intellectual performance. Arch Neurol 1978; 35:17–21
23. Wallace SJ: Prognosis after prolonged unilateral febrile convulsions. In Akimoto H, Kazamatsuri H, Seino M, Ward A (eds): Advances in Epileptology: The XIII Epilepsy International Symposium. New York, Raven Press, 1982, pp 97–99
24. Gerber MA, Berliner BS: The child with a "simple" febrile seizure: Appropriate diagnostic evaluation. Am J Dis Child 1981; 135:431–433
25. Committee on Infectious Diseases: Aspirin and Reye syndrome. Pediatrics 1982; 69:810–812
26. Bettis DB, Ater SB: Febrile seizures: Emergency department diagnosis and treatment. J Emerg Med 1985; 2:341–348
27. Camfield PR: Treatment of status epilepticus in children. Can Med Assoc J 1983; 128:671
28. Milligan NM, Dhillon S, Griffiths A, et al: A clinical trial of single dose rectal and oral administration of diazepam for the prevention of serial seizures in adult epileptic patients. J Neurol Neurosurg Psychiatr 1984; 47:235–240
29. Lee K, Tandorf K, Hvorslev V: Prophylactic treatment with valproic acid or diazepam in children with febrile convulsions. Acta Paediatr Scand 1986; 75:593–597
30. Knudsen FU: Effective short-term diazepam prophylaxis in febrile convulsions. J Pediatr 1985; 106:487–490
31. Rosman NP: Febrile seizures. Emerg Med Clin North Am 1987; 5:719–737
32. Dreifuss FE, Santilli N, Longer DH, et al: Valproic acid hepatic fatalities: A retrospective review. Neurology 1987; 37:379–385
33. Joffe A, McCormick M, DeAngelis C: Which children with febrile seizures need lumbar puncture? Am J Dis Child 1982; 137:1153–1156
34. Vining EPG, Freeman JM: Discussion and explanation of seizures to the parents and child. Pediatr Ann 1985; 14:7737–7739
35. Wolf SM, Carr A, Davis DC, et al: The value of phenobarbital in the child who has had a single febrile seizure: A controlled prospective study. Pediatrics 1977; 59:378–385
36. Camfield PR, Camfield CS, Shapiro SH, et al: The first febrile seizure: Antipyretic instruction plus either phenobarbital or placebo to prevent recurrence. J Pediatr 1980; 97:16–21
37. Wolf SM, Forsythe A: Behavior disturbance, phenobarbital, and febrile seizures. Pediatrics 1978; 61:728–731
38. Bacon CJ, Hierons AM, Mucklow JC, et al: Placebo-controlled study of phenobarbitone and phenytoin in the prophylaxis of febrile convulsions. Lancet 1982; 2:600–604
39. Anthony JH, Hawk SH: Phenobarbital compared with carbamazepine in prevention of recurrent febrile convulsions. Am J Dis Child 1983; 173:892–895
40. Davidson S, Falconer MA: Outcome of surgery in 40 children with temporal lobe epilepsy. Lancet 1975; 1:1260–1263
41. Hauser WA: The natural history of febrile seizures. In Nelson KB, Ellenberg JH (eds): Febrile Seizures. New York, Raven Press, 1981, pp 5–17
42. Ellenberg JH, Nelson KB: Long-term clinical trials on the use of prophylaxis for prevention of recurrences of febrile seizures and epilepsy. In Nelson KB, Ellenberg JH (eds): Febrile Seizures. New York, Raven Press, 1981, pp 267–278