

---

## *Clinical Guideline*

---

### Clinical Guideline on Management of Febrile Convulsion

V **WONG**, MHK **HO**, NP **ROSMAN**, Y **FUKUYAMA**,  
CY **YEUNG**, KH **CHAN**, MSC **WONG**, CM **VERITY**, CF **CHENG**

---

#### **Guideline Development Panel**

##### Local

Prof. V Wong (Chairman)  
Dr. KH Chan  
Dr. CF Cheng  
Dr. MHK Ho  
Dr. MSC Wong  
Prof. CY Yeung

##### Overseas

Prof. Y Fukuyama  
Prof. NP Rosman  
Dr. CM Verity

#### **Guideline Review Panel**

Dr. CW Chan  
Dr. KY Chan  
Dr. P Ip  
Dr. YC Tsao

#### **Date of Endorsement**

1st September, 2001

#### **Date of Review**

1st September, 2003

---

#### **Disclaimer**

This guideline is prepared by the Hong Kong College of Paediatricians and the authors, according to the state of medical knowledge obtained and existing at the time of compilation. Although all information and opinions expressed in this guideline were obtained from medical sources believed to be reliable and in good faith, no representation or warranty, express or implied, is made as to its accuracy or completeness. This guideline is for general guidance only and designed to provide information to assist decision making. The recommendations are valid only as at the date of issue and subject to change without further notice. Paediatricians should utilize and rely on their up-to-date medical knowledge, clinical data of the patients and their own clinical judgment in applying the recommendations in this document to the management of individual patients.

---

## Explanatory Notes on Level of Evidence

The definition of levels and types of evidence is adapted from the US Agency for Health Care Policy and Research 1992 (AHCPR). This is also recommended and used by the Royal College of Paediatrics and Child Health (RCPCH).

### Levels of evidence

<i>Level</i>	<i>Type of evidence (based on AHCPR 1992)</i>
Ia	Evidence obtained from meta-analysis of randomised controlled trials
Ib	Evidence obtained from at least one randomised controlled trial
IIa	Evidence obtained from at least one well-designed controlled study without randomisation
IIb	Evidence obtained from at least one other type of well-designed quasi-experimental study
III	Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case control studies
IV	Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities

## Introduction

Febrile convulsion (FC) is the most common convulsive disorder in children. Those who advocate therapy for FC have been concerned that such convulsion may lead to recurrent febrile convulsions, epilepsy, or perhaps even to brain injury. These concerns indeed also cause a lot of parental anxiety.

The Working Group on Development of Clinical Practice Guidelines of the Hong Kong College of Paediatricians has designated Professor Virginia Wong as the Chairman to recruit panel members to review the literature in order to derive evidence-based recommendations for the management of febrile convulsion.

### The Aims are:

1. To improve the paediatric practitioner's understanding of the natural history of febrile convulsion.
2. To provide reasonable guidelines for the management of simple febrile convulsion based on current scientific evidence.

## Content

1. Definition
  - 1.1 Simple febrile convulsion
  - 1.2 Complex febrile convulsion
2. Acute management of febrile convulsion
3. Hospital admission
4. Investigations

4.1 Lumbar puncture

4.2 EEG

4.3 Blood

4.4 Neuroimaging

5. Management of fever

6. Therapeutic Intervention for Recurrent Febrile Convulsions

6.1 Intermittent *therapy with diazepam* during an acute attack

6.2 Long-term anticonvulsant prophylaxis

7. Prognosis

8. Immunization

9. Parental education

10. Conclusion

### 1) Definition

Febrile convulsion (FC) is defined as convulsion occurring in a child, aged *6 months to 5 years\**, associated with fever but without evidence of intracranial infection or defined cause, who is otherwise neurologically normal. Convulsions with fever in children who have suffered a previous non-febrile convulsion are excluded.

1.1 "Simple febrile convulsion" is defined as primary generalized convulsion lasting less than 15 minutes and not recurring within 24 hours.

1.2 "Complex febrile convulsion" is defined as focal or prolonged (>15 minutes), and/or more than one convulsion in 24 hours.

- 1.3 "Febrile Status" is a convulsion duration of >30 minutes, either one long lasting convulsion or a series of shorter convulsions, without regaining consciousness interictally.

N.B. 1 Febrile Convulsion should be distinguished from "convulsion with fever", which includes any convulsion in any child with fever of any cause. Thus, children with meningitis, encephalitis, or cerebral malaria do not have febrile convulsions but have convulsions with fever. The same is true for children with severe neurologic disorders and/or severe mental retardation.

N.B.2 The number of so-called "reflex anoxic convulsions" presenting as febrile convulsions is unknown. It seems to be a syncopal type of anoxic convulsion resulting from vagal-induced bradycardia or asystole with reduced cerebral blood flow. The provoking factor may be fever, thus mimicking a febrile convulsion.

\* According to classification of International League Against Epilepsy (1989) – the age was "1 month" instead of "6 months".

## 2) Acute Management of Febrile Convulsion:

- Maintain a clear airway.
- Protect the child from injury.
- Place the child in a semi-prone position.
- Loosen clothing or remove excess clothing.
- Give oxygen if available.
- Apply suction for nasal or oral secretions if facility available
- Treat fever by sponging with tepid water and antipyretics (e.g. acetaminophen).

(Level Ib)

- Monitor vital signs.
- If facilities and medications are available – administer rectal diazepam 0.2-0.5 mg/kg/dose if convulsion lasts for more than 5 minutes.

(Level IV)

- Administer intravenous anticonvulsant if the child is still convulsing for >15 minutes (diazepam, lorazepam or phenobarbital), (preferably in the listed order), and depending on the availability of anticonvulsant.

- a. Intravenous **diazepam, 0.2-0.5 mg/kg/dose**

(maximum rate: 1-2 mg/minute) to a maximum dose of **2-4 mg** in an infant or **5-10 mg** in the older child. The same dose can be repeated every 10 to 30 minutes to a total of **3 doses**, if necessary.

- b. Intravenous **lorazepam, 0.05-0.10 mg/kg/dose** (maximum rate: 1 mg/minute) to a maximum dose of **4 mg** can be given; with an additional 0.05 mg/kg 10 minutes later if needed.
- c. Intravenous **phenobarbital** in a dose of **15-20 mg/kg** (rate: 30 to 100 mg/minute); with half of the initial dose repeated in an hour if necessary. **(Level IV)**

## 3) Hospital Admission

Children should preferably be observed for several hours after a febrile convulsion. If they are clinically stable with cause of fever identified and treated, they may be sent home. However, follow-up care must be assured. Hospital admission is individualized. It depends on the experience of the practitioner, specific clinical situation and family circumstances.

- ◆ After a **first** convulsion, the following factors favor admission **(Level IV)**
  - complex convulsion:
    - lasting longer than 15 minutes or
    - with focal features or
    - repeated in 24 hours of first convulsion or
    - with incomplete recovery after 1 hour;
  - the paediatrician is suspicious of possibility of meningitis and encephalitis;
  - a child aged <18 months;
  - anxious parents or inadequate home care.

## 4) Investigations

### 4.1) Role of Lumbar Puncture (LP)

LP needs to be considered in every child who has a febrile convulsion in whom there is even a small possibility of acute bacterial meningitis. However, most febrile convulsions associated with meningitis are complex.

(Level IV)

### When to Do a Lumbar Puncture ?

The decision should be taken by an experienced paediatrician who should decide on clinical grounds whether LP is unnecessary for a younger child. In case of

doubt, LP should be performed. If LP is not performed, the paediatrician is advised to review the case within a few hours. A convulsing child who is comatosed should receive neuroimaging before LP. (Level IV)

- ❑ In every child with a first febrile convulsion that is complex.
- ❑ Also, every child <1 year of age with a febrile convulsion should be advised to have a LP, since the clinical signs and symptoms of meningitis may be minimal or absent at this age.
- ❑ Between 12-18 months, LP should be considered because the clinical signs and symptoms of meningitis may be subtle.
- ❑ In a child >18 months, LP should be done in the presence of meningeal signs and symptoms or whenever the history or examination suggests the presence of an intracranial infection.
- ❑ In infants and children with febrile convulsions who have received antibiotic treatment, LP should be strongly considered, since such treatment can mask evidence of meningitis.

#### 4.2) EEG (Level IV)

- EEG is rarely indicated in the management of a simple febrile convulsion.  
[N.B. In 90% of children following a febrile convulsion, an EEG on that day shows slow wave activities which usually disappear by 7 to 10 days.]

#### 4.3) Blood (Level IV)

- In addition to drawing a blood specimen for glucose in a child who is drowsy, if facilities are available, one should obtain toxicology screen, electrolytes and urea.

#### 4.4) Neuroimaging (Level IV)

Neuroimaging is **not** necessary in most cases, but there are exceptions, e.g. in a child with:

- papilloedema,
- cranial nerve palsies (e.g. 6th nerve palsy),
- other persisting focal neurological signs (e.g. hemiparesis) or
- marked depression in mental status, then neuroimaging is probably appropriate.

#### 5) Management of Fever (Level Ib)

- ❑ There is **no** evidence that antipyretic treatment *prevents* the recurrence of febrile convulsions.
- ❑ Fever should be treated in order to promote the comfort of the child and to prevent dehydration.
- ❑ Use of antipyretic drug is effective and paracetamol or ibuprofen is advised. (Level Ib)
- ❑ An adequate fluid intake is advisable.

#### 6) Therapeutic Intervention for Recurrent Febrile Convulsions

##### 6.1) Intermittent Therapy with Diazepam During an Acute Attack

*If given in sufficient doses, it is likely to be effective in preventing febrile convulsion recurrence.* (Level Ib)

- ❑ **Rectal diazepam** (Level IIa)
  - Is advisable for convulsions lasting >5 minutes.
  - Parents should be advised not to give rectal diazepam if the convulsion has stopped.
  - Rectal diazepam can prevent febrile convulsions when given at the onset of fever. However, this has **not** been studied in a controlled, double-blind fashion, but proven by randomized control trial. (Level Ib)
  - Rectal diazepam is useful to prevent a recurrence when used in an early stage of febrile episode (at the time of up-going fever over 38.5°C).
- ❑ **Intermittent diazepam prophylaxis seems to be effective in reducing the recurrence rate provided:** (Level Ib)
  - sufficient doses are given
  - compliance problems are minimized and very low risk children are left untreated
  - **suggested doses for prophylaxis = 0.5 mg/kg administered orally, or rectally every 12 hr whenever the rectal temperature is >38.5°C, with a maximum of 4 consecutive doses to avoid accumulation of the drug.**

[N.B. Side effects of diazepam include ataxia, lethargy and irritability. When children are given intermittent diazepam at the time of fever, one should be alert to monitor the child

regularly in case the underlying infection may be masked due to lethargy from the effect of diazepam.]

#### 6.2) Long-term Anticonvulsant Prophylaxis

- ❑ **No** definitive evidence that prophylactic treatment of febrile convulsions with anticonvulsants can prevent later epilepsy.  
There is no prospective study that looked into this important question.
- ❑ There had been traditional advocate of using long-term anticonvulsant prophylaxis (phenobarbitone in 1970 or sodium valproate in early 1980s). However, this is currently **not** advised due to side effects. Other anticonvulsants (carbamazepine, phenytoin) are not useful.  
(Level Ia)
- ❑ There is almost universal agreement that long-term anticonvulsant prophylaxis is justified only in highly selected case (based on clinical circumstances and the judgement at the element), if at all, due to side effects.

#### 7) Prognosis

The prognosis of febrile convulsion in terms of intellectual outcome is good. Most children with febrile convulsions do not develop epilepsy. (Level IIa)

#### Recurrence Risk of Febrile Convulsion (Level IIa)

- Risk of recurrence is 50% if the febrile convulsion occurs in the first year of life.
- Major predictor for recurrence of febrile convulsion is early age of onset.

#### Risk of Intellectual Deficit (Level IIa)

- Only among those with pre-existing neurological or developmental abnormality.
- And in those who developed subsequent afebrile convulsions.

#### Risk Factors for Developing Epilepsy (Level IIa)

- Preexisting neurological abnormality.
- Family history of afebrile convulsion.
- Complex first febrile convulsion.

#### 8) Immunization (Level IV)

None of the current standard vaccinations are contraindicated.

#### DTP

Diphtheria, tetanus, pertussis, and poliomyelitis immunization have already been given to children at 2-4 months. Thus this should be before the usual onset of febrile convulsions. If a child has febrile convulsion before immunization against diphtheria, pertussis, and tetanus due to delay in immunization, the child could be immunized provided the parents have been instructed about the management of fever and the use of rectal diazepam. (Level IV)

#### MMR

There is no contraindication to Measles, Mumps and Rubella (MMR) vaccination for children with history of febrile convulsion. Parents should be advised about the management of fever after giving MMR vaccination. Keep the child under close observation. Rectal diazepam is recommended to be given in case convulsion lasting >5 minutes occurs. (Level IV)

#### 9) Parental Education

Studies have shown that many parents witnessing a child's first convulsion thinks that their child is dying or is already dead. Try to decrease parental anxiety by counseling. Reassurance and education is thus very important. Instructions on the future management of possible recurrences should be given with emphasis on practical issues of how to manage a child with febrile convulsion at the scene. (Level IV)

Information to be provided to parents:

- ❑ Most febrile convulsions have an excellent prognosis.
- ❑ Effective therapy to prevent recurrence is available but potential side effects suggest against such prophylaxis.
- ❑ No evidence that any therapy will alleviate possibility of future epilepsy.

#### 10) Conclusion

The purpose of this clinical guideline is to provide a medical framework for evaluation and treatment of simple febrile convulsion. In individual cases, the paediatrician's clinical judgement is important to manage the child's clinical condition. Clinical guidelines serve a role in which audit and review of current clinical practice can take place. Updating and revisions of these guidelines are expected in accordance with newer information.

*Recommended Checklist for Paediatricians/Family Physicians*

- An accurate description of the convulsion, including its duration
- Information about the nature of the episode
- A record about the family history with regard to febrile and non-febrile convulsions
- The age at first convulsion
- The temperature on admission
- Whether signs of meningitis are present or absent
- An assessment of the cause of the fever
- The child's neurodevelopmental state when recovered
- The blood glucose concentration, if the child was seen during a convulsion
- Other serum chemistries as indicated (electrolytes, calcium)
- An estimate of the likely prognosis, advice to the parents about what to do if further convulsions occur, and advice about future immunization
- What the parents were told at admission and before discharge

## References

### General

1. Addy DP. Nosology of febrile convulsions. *Arch Dis Child* 1986; 61:318-20.
2. Aicardi J. Febrile Convulsions. In: *Epilepsy in Children* (2nd Ed), Aicardi J, Raven press, New York 1994, Chapter 15:253-275.
3. Akpede GO, Sykes RM. Convulsions with fever as a presenting feature of bacterial meningitis among preschool children in developing countries. *Dev Med Child Neurol* 1992;34:524-9.
4. Practice Parameter: long-term treatment of the child with simple febrile seizures. American Academy of Pediatrics, Committee on Quality Improvement, Subcommittee on Febrile Seizures. *Pediatrics* 1999;103(6 Pt 1):1307-9.
5. Febrile Seizures: long-term management of children with fever-associated seizures. Summary of an NIH consensus statement. *Br Med J* 1980;281:277-9.
6. Baker N. Febrile Convulsions. *J Paediatr Obstetr Gynaecol* 1995; 10-12.
7. Berg AT, Shinnar S, Hauser WA, et al. A prospective study of recurrent febrile seizures. *N Engl J Med* 1992;327:1122-7.
8. Berg AT, Shinnar S. Complex febrile seizures. *Epilepsia* 1996; 37:126-33.
9. Berg AT. Are febrile seizures provoked by a rapid rise in temperature? *Am J Dis Child* 1993;147:1101-3.
10. Bethune P, Gordon K, Dooley J, Camfield C, Camfield A. Which child will have a febrile seizure? *Am J Dis Child* 1993;147: 35-9.
11. Burhanoglu M, Tutuncuoglu S, Coker C, Tekgul H, Ozgur T. Hypozinaemia in febrile convulsion. *Eur J Pediatr* 1996;155: 498-501.
12. Proposal for revised classification of epilepsies and epileptic syndromes. Commission on Classification and Terminology of International League Against Epilepsy. *Epilepsia* 1989;32:389-99.
13. Guidelines for epidemiologic studies on epilepsy. Commission on Epidemiology and Prognosis, International League Against Epilepsy. *Epilepsia* 1993;34:592-6.
14. Fukuyama Y, Seki T, Ohtsuka C, Miura H, Hara M. Practical guidelines for physicians in the management of febrile seizures. *Brain Dev* 1996;18:479-84.
15. Fukuyama Y. Proceedings of the First National Meeting of the Study Group on Seizures in Infancy and Early Childhood. Tokyo, April 4, 1998. *Brain Dev* 1998;20:550-8.
16. Germano IM, Zhang YF, Sperber EF, Moshe SL. Neuronal migration disorders increase susceptibility to hyperthermia-induced seizures in developing rats. *Epilepsia* 1996;37:902-10.
17. Green AL, Macfaul R. Duration of admission for febrile convulsions? *Arch Dis Child* 1985;60:1182-4.
18. Hirtz DG. Febrile seizures. *Pediatr Rev* 1997;18:5-8.
19. Hirtz DG. Generalized tonic-clonic and febrile seizures. *Pediatr Clin North Am* 1989;36:365-82.
20. Johnson EW, Dubovsky J, Rich SS, et al. Evidence for a novel gene for familial febrile convulsions, FEB2, linked to chromosome 19p in an extended family from the Midwest. *Hum Mol Genet* 1998;7:63-7.
21. 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. *Br Med J* 1991;303:634-6.
22. Kondo K, Nagafuji H, Hata A, Tomomori C, Yamanishi K. Association of human herpesvirus 6 infection of the central nervous system with recurrence of febrile convulsions. *J Infect Dis* 1993;167:1197-200.
23. Knudsen FU. Frequent febrile episodes and recurrent febrile convulsions. *Acta Neurol Scand* 1988;78:414-7.
24. Lennox-Buchthal MA. Febrile convulsions. A reappraisal. *Electroencephalogr Clin Neurophysiol* 1973;32(Suppl 1):1-138.
25. Lessell S, Torress JM, Kurland LT. Seizure disorders in a Guamanian village. *Arch Neurol* 1962;7:37-44.
26. Lloyd GER. Hippocratic writings. Harmondsworth, England. Penguin Books 1978:1850.
27. Millichap JG. Febrile Convulsions. Macmillan, New York 1968: 1-222.
28. Febrile seizures: long-term management of children with fever-associated seizures. Summary of an NIH consensus statement. *Br Med J* 1980;281:277-9.
29. Nelson KB, Ellenberg JH. Consensus statement on febrile seizures. In: *Febrile Seizures*. New York, Raven Press 1981: 301-306.
30. Nelson KB, Ellenberg JH. Febrile seizures. In: Dreifuss FE (ed): *Pediatric Epileptology*. Boston, John Wright, 1983:173-198.
31. Nelson KB, Ellenberg JH. Prenatal and perinatal antecedents of febrile seizures. *Ann Neurol* 1990;27:127-31.
32. Nelson KB, Hirtz DG. Febrile seizures. In: *Pediatric Neurology: Principles and Practice*, Chapter 34:565-569, edited by KF Swaiman, 2nd ed., CV Mosby Co., St. Louis 1994.

33. NIH Consensus Statement. Febrile seizures – long-term management of children with fever-associated seizures – NIH consensus development conference. *Neuropediatrics* 1980;11: 196-201.
34. Offringa M, Derksen-Lubsen G, Bossuyt PM, Lubsen J. Seizure recurrence after a first febrile seizure: a multivariate approach. *Dev Med Child Neurol* 1992;34:15-24.
35. Offringa M. Seizures associated with fever: current management controversies. *Seminars in Pediatric Neurology* 1994;1:90-101.
36. Oppenheimer EY, Rosman NP. Recurring seizures (status epilepticus). In: *Manual of Emergency Pediatrics:105-111*, edited by RM Reece, 4th ed., W.B. Saunders Co., Philadelphia 1992.
37. Rosman NP, Peterson DB, Kaye EM, Colton T. Seizures in bacterial meningitis: prevalence, patterns, pathogenesis and prognosis. *Pediatr Neurol* 1985;1:278-85.
38. Rosman NP. Evaluation and management of febrile seizures. *Curr Opin Pediatr* 1989;1:318-23.
39. Rosman NP. Febrile seizures. *Emerg Med Clin North Am* 1987; 5:719-37.
40. Stenklyft PH, Carmona M. Febrile Seizures. *Emerg Med Clin North Am* 1994;12:989-97.
41. Suga S, Yoshikawa T, Asano Y, et al. Clinical and virological analyses of 21 infants with exanthem subitum (roseola infantum) and central nervous system complications. *Ann Neurol* 1993; 33:597-603.
42. Tsuboi T. Epidemiology of febrile and afebrile convulsions in children in Japan. *Neurology* 1984;34:175-81.
43. van Stuijvenberg M, Moll HA, Steyerberg EW, van Gijssel EN, Moons KG, Derksen-Lubsen G. The duration of febrile seizures and peripheral leukocytosis. *J Pediatr* 1998;133:557-8.
44. Wallace RH, Berkovic SF, Howell RA, Sutherland GR, Mulley JC. Suggestion of a major gene for familial febrile convulsions mapping to 8q13-21. *J Med Genet* 1996;33:308-12.
45. Wallace SJ. The child with febrile seizures. *John Wright* 1988: 1-182.

#### Lumbar Puncture

46. American Academy of Neurology, Practice Handbook. Practice Parameters: lumbar puncture. Report of the Quality Standards Subcommittee. 2/22/93:149-155.
47. Green SM, Rothrock SG, Clem KJ, Zurcher RF, Mellick L. Can seizures be the sole manifestation of meningitis in febrile children? *Pediatrics* 1993;92:527-34.
48. Nozicka C. Lumbar puncture and the first simple febrile seizure. *Pediatrics* 1997;99:306-7.
49. Offringa M, Beishuizen A, Derksen-Lubsen G, Lubsen J. Seizures and fever: can we rule out meningitis on clinical grounds alone? *Clin Pediatr* 1992;31:514-22.

#### EEG

50. Doose H, Ritter K, Volzke E. EEG longitudinal studies in febrile convulsions. Genetic aspects. *Neuropediatrics* 1983;14:81-7.
51. Koyama A, Matsui T, Sugisawa T. Febrile convulsions in northern Japan: a quantitative and qualitative analysis of EEG and clinical findings. *Acta Neurol Scand* 1991;83:411-7.
52. Kuturec M, Emoto SE, Sofijanov N, et al. Febrile seizures: is the EEG a useful predictor of recurrences? *Clin Pediatr* 1997; 36:31-6.
53. Martinez Menendez B, Simon de las Heras R, de la Pena Mayor P, Perez Sempere A, Alvarez Tejerina J, Mateos Beato F. Febrile seizures: is EEG useful? *An Esp Pediatr* 1999;50:126-8.

54. Stores G. When does an EEG contribute to the management of febrile seizures? *Arch Dis Child* 1991;66:554-7.

#### Neuroradiology

55. 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* 1996;97:769-72; discussion: 773-5.
56. 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* 1996;97: 769-72.
57. VanLandingham KE, Heinz ER, Cavazos JE, Lewis DV. Magnetic resonance imaging evidence of hippocampal injury after prolonged focal febrile convulsions. *Ann Neurol* 1998;43: 413-26.

#### Recurrence Rate

58. el-Radhi AS, Banajeh S. Effect of fever on recurrence rate of febrile convulsions. *Arch Dis Child* 1989;64:869-70.

#### Risk Factors

59. al-Eissa YA. Febrile seizures: rate and risk factors of recurrence. *J Child Neurol* 1995;10:315-9.
60. Annegers JF, Hauser WA, Shirts SB, Kurland LT. Factors prognostic of unprovoked seizures after febrile convulsions. *N Engl J Med* 1987;316:493-8.
61. Berg AT, Shinnar S, Hauser WA, Leventhal JM. Predictors of recurrent febrile seizures: a metaanalytic review. *J Pediatr* 1990;116:329-37.
62. Berg AT, Shinnar S, Shapiro ED, Salomon ME, Crain EF, Hauser WA. Risk factors for a first febrile seizure: a matched case-control study. *Epilepsia* 1995;36:334-41.
63. Cassano PA, Koepsell TD, Farwell JR. Risk of febrile seizures in childhood in relation to prenatal maternal cigarette smoking and alcohol intake. *Am J Epidemiol* 1990;132:462-73.
64. Ferry PC. Risk factors in febrile seizures. Any surprises? *Am J Dis Child* 1993;147:14-39.
65. Offringa M, Bossuyt PM, Lubsen J, et al. Risk factors for seizure recurrence in children with febrile seizures: a pooled analysis of individual patient data from five studies. *J Pediatr* 1994;124:574-84.
66. Rantala H, Uhari M. Risk factors for recurrences of febrile convulsions. *Acta Neurol Scand* 1994;90:207-10.
67. van Esch A, Steyerberg EW, Berger MY, Offringa M, Derksen-Lubsen G, Habbema JD. Family history and recurrence of febrile seizures. *Arch Dis Child* 1994;70:395-9.

#### Prognosis

68. Annegers JF, Blakley SA, Hauser WA, Kurland LT. Recurrence of febrile convulsions in a population-based cohort. *Epilepsy Res* 1990;3:209-16.
69. Berg AT, Shinnar S, Darefsky AS, et al. Predictors of recurrent febrile seizures. A prospective cohort study. *Arch Pediatr Adolesc Med* 1997;151:371-8.
70. Berg AT, Shinnar S. Unprovoked seizures in children with febrile seizures: short-term outcome. *Neurology* 1996;47:562-8.
71. Ellenberg JH, Nelson KB. Febrile seizures and later intellectual performance. *Arch Neurol* 1978;35:17-21.
72. Hauser WA. The natural history of febrile seizures. In Nelson

- KB and Ellenberg JH (eds): Febrile Seizures. New York, Raven Press 1981:5-17.
73. Knudsen FU. Febrile seizures – treatment and outcome. *Brain Dev* 1996;18:438-49.
  74. Knudsen FU. Febrile seizures: treatment and prognosis. *Epilepsia* 2000;41:2-9.
  75. Knudsen FU, Paerregaard A, Andersen R, Andersen J. Long-term prognosis in febrile convulsion with and without prophylaxis. *Ugeskr Laeger* 1997;159:3598-602.
  76. Knudsen FU, Paerregaard A, Andersen R, Andersen J. Long term outcome of prophylaxis for febrile convulsion. *Arch Dis Child* 1996;74:13-8.
  77. Nelson KB, Ellenberg JH. Prognosis in children with febrile seizures. *Pediatrics* 1978;61:720-7.
  78. Nelson KB, Ellenberg JH. Section discussion on consequences of febrile seizures. In: Febrile Seizures. New York, Raven Press 1981:35-42.
  79. Smith JA, Wallace SJ. Febrile convulsions: intellectual progress in relation to anticonvulsant therapy and to recurrence of fits. *Arch Dis Child* 1982;57:104-7.
  80. Tarkka R, Rantala H, Uhari M, Pokka T. Risk of recurrence and outcome after the first febrile seizure. *Pediatr Neurol* 1998; 18:218-20.
  81. Tsuboi T, Endo S, Iida N. Long-term follow-up of a febrile convulsion cohort. *Acta Neurol Scand* 1991;84:369-73.
  82. Verity CM, Butler NR, Golding J. 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)* 1985;290:1307-10.
  83. Verity CM, Butler NR, Golding J. 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)* 1985;290:1311-5.
  84. Verity CM, Greenwood R, Golding J. Long-term intellectual and behavioral outcomes of children with febrile convulsions. *N Engl J Med* 1998;338:1723-8.
- Epilepsy
85. Annegers JF, Hauser WA, Elveback LR, Kurland T. The risk of epilepsy following febrile convulsions. *Neurology* 1979; 29:297-303.
  86. Berg AT. Febrile seizures and epilepsy: the contributions of epidemiology. *Pediatr Perinatol Epidemiol* 1992;6:145-52.
  87. Camfield P, Camfield C, Gordon K, Dooley J. What types of epilepsy are preceded by febrile seizures? A population-based study of children. *Dev Med Child Neurol* 1994;36:887-92.
  88. Cendes F, Andermann F, Dubeau F, et al. Early childhood prolonged febrile convulsions, atrophy and sclerosis of mesial structures, and temporal lobe epilepsy: an MRI volumetric study. *Neurology* 1993;43:1083-7.
  89. Fernandez G, Effenberger O, Vinz B, et al. Hippocampal malformation as a cause of familial febrile convulsions and subsequent hippocampal sclerosis. *Neurology* 1998;50:909-17.
  90. Hamati-Haddad A, Abou-Khalil B. Epilepsy diagnosis and localization in patients with antecedent childhood febrile convulsions. *Neurology* 1998;50:917-22.
  91. Nelson KB, Ellenberg JH. Predictors of epilepsy in children who have experienced febrile seizures. *N Engl J Med* 1976; 295:1029-33.
  92. Rapkin RH. Relation of epilepsy and febrile seizures. *Pediatr Rev* 1993;14:190
  93. Shinnar S, Pellock JM, Moshe SL, et al. In whom does status epilepticus occur: age-related differences in children. *Epilepsia* 1997;38:907-14.
  94. Shinnar S. Prolonged febrile seizures and mesial temporal sclerosis. *Ann Neurol* 1998;43:411-2.
  95. Sloviter RS, Pedley TA. Subtle hippocampal malformation: importance in febrile seizures and development of epilepsy. *Neurology* 1998;50:846-9.
  96. Wolf SM, Forsythe A. Epilepsy and mental retardation following febrile seizures in childhood. *Acta Paediatr Scand* 1989;78: 291-5.
- Treatment
97. Addy DP. Prophylaxis and febrile convulsions. *Arch Dis Child* 1981;56:81-3.
  98. American Academy of Pediatrics. Behavioural and cognitive effects of anticonvulsant therapy. Committee on Drugs. *Pediatrics* 1995;96:538-40.
  99. Baumann RJ. Technical report: treatment of the child with simple febrile seizures. *Paediatrics* 1999;103:e86.
  100. Baumann RJ, Duffner PK. Treatment of children with simple febrile seizures: the AAP practice parameter. *American Academy of Pediatrics. Pediatr Neurol* 2000;23:11-7.
  101. Freeman JM, Holmes GL. Should uncomplicated seizures be treated? Point – counterpoint. *Curr Probl Pediatr* 1994;24:139-48.
  102. Freeman JM, Vining EP. Decision making and the child with febrile seizures. *Pediatr Rev* 1992;13:298-304.
  103. Freeman JM. Just say no! Drugs and febrile seizures. *Pediatrics* 1990;86:624.
  104. Freeman JM. The best medicine for febrile seizures. *N Engl J Med* 1992;327:1161-3.
  105. Newton RW, McKinlay I. Subsequent management of children with febrile convulsions. *Dev Med Child Neurol* 1988;30:402-6.
  106. Ramakrishnan K, Thomas K. Long term prophylaxis of febrile seizures. *Indian J Pediatr* 1986;53:397-400.
  107. Rosman NP. The case for treating febrile seizures. *Contemporary Pediatrics* 1992;9:12-34
  108. Sweeney A, Gibbs J, Monteil F, Appleton R, Choonara L. The management of febrile seizures in the Mersey Region. *Dev Med Child Neurol* 1996;38:578-84.
  109. Trimble MR, Cull CA. Antiepileptic drugs, cognitive function, and behavior in children. *Cleve Clin J Med* 1989;56 Suppl Pt 1: S140-6.
  110. Watanabe T. Pros and cons of treatments and studies of recurrent febrile seizures. *J Pediatr* 1998;133:715.
- Acetaminophen
111. Camfield PR, Camfield CS, Shapiro SH, Cummings C. The first febrile seizure – antipyretic instruction plus either phenobarbital or placebo to prevent recurrence. *J Pediatr* 1980;97:16-21.
  112. Schnaiderman D, Lahat E, Sheefer T, Aladjern M. Antipyretic effectiveness of acetaminophen in febrile seizures: ongoing prophylaxis versus sporadic usage. *Euro J Pediatr* 1993;152: 747-9.
  113. Uhari M, Rantala H, Vainionpaa L, Kurttila R. Effect of acetaminophen and of low intermittent doses of diazepam on prevention of recurrence of febrile seizures. *J Pediatr* 1995;126: 991-5.
- Diazepam (Rectal)
114. Agurell S, Berlin A, Ferngren H, Hellstorm B. Plasma levels of



- diazepam after parenteral and rectal administration in children. *Epilepsia* 1975;16:277-83.
115. Dianese G. Prophylactic diazepam in febrile convulsions. *Arch Dis Child* 1979;54:244-5.
  116. Dreifuss FE, Rosman NP, Cloyd JC, et al. A comparison of rectal diazepam gel and placebo for acute repetitive seizures. *N Engl J Med* 1998;338:1869-75.
  117. McKinlay I, Newton R. Intention to treat febrile convulsions with rectal diazepam, valproate, or phenobarbitone. *Dev Med Child Neurol* 1989;31:617-25.
  118. Shirai H, Miura H, Sunaoshi W. A clinical study on the effectiveness of intermittent therapy with rectal diazepam suppositories for the prevention of recurrent febrile convulsions: a further study. *Journal of Japanese Epilepsy Society* 1988;6:1-10.
- Diazepam (Oral)
119. Autret E, Billard C, Bertrand P, Motte J, Pouplard F, Jouville AP. Double-blind, randomized trial of diazepam versus placebo for prevention of recurrence of febrile seizures. *J Pediatr* 1990;117:490-4.
  120. Hohjo M, Miura H, Minagawa K, et al. A clinical study on the effectiveness of intermittent therapy with oral diazepam syrups for the prevention of recurrent febrile convulsions: a preliminary report. *Brain Development* 1986;8:559-60.
  121. Knudsen FU. Effective short-term diazepam prophylaxis in febrile convulsions. *J Pediatr* 1985;106:487-90.
  122. Knudsen FU. Intermittent diazepam prophylaxis in febrile convulsions. Pros and cons. *Acta Neurol Scand Suppl* 1991;83:1-24.
  123. Knudsen FU. Recurrence risk after first febrile seizure and effect of short-term diazepam prophylaxis. *Arch Dis Child* 1985;60:1045-9.
  124. Miceli Sopo S, Pesaresi MA, Colestini E, Stabile A. Short-term prophylaxis of febrile convulsions. *Acta Pediatr Scand* 1991;80:248-9.
  125. Minagawa K, Mizuno S, Shirai H, Miura H. A pharmacokinetic study on the effectiveness of intermittent oral diazepam in the prevention of recurrent febrile convulsions. *No To Hattatsu* 1985;17:162-7.
  126. Nuzez-Lopez LC, Espinosa-Garcia E, Hernandez-Arbelaez E, et al. Efficacy of diazepam to prevent recurrences in children with a first febrile convulsion. *Acta Neuropediatrics* 1995;1:187-95.
  127. Thorn I. Prevention of recurrent febrile seizures: intermittent prophylaxis with diazepam compared with continuous treatment with phenobarbital. In Nelson KB and Ellenberg JH (eds): *Febrile Seizures*. New York, Raven Press, 1981:119-26.
- Phenobarbitone
128. Addy DP. Phenobarbitone and febrile convulsions. *Arch Dis Child* 1990;65:921.
  129. Bacon CJ, Hierous AM, Mucklow JC, Webb JK, Rawlins MD, Weightman D. Placebo-controlled study of phenobarbitone and phenytoin in the prophylaxis in febrile convulsions. *Lancet* 1981;2:600-4.
  130. Farwell JR, Lee YJ, Hirtz DG, Sulzbacher SI, Ellenberg JH, Nelson KB. Phenobarbital for febrile seizure recurrence. *N Engl J Med* 1990;322:364-9.
  131. Farwell JR, Lee YJ, Hirtz DG, Sulzbacher SI, Ellenberg JH, Nelson KB. Phenobarbital for febrile seizure recurrence. Erratum in: *N Engl J Med* 1992;326:144.
  132. Herranz JL, Armijo JA, Arteaga R. Effectiveness and toxicity of phenobarbital, primidone, and sodium valproate in the prevention of febrile convulsions, controlled by plasma levels. *Epilepsia* 1984;25:89-95.
  133. Mamelle N, Mamelle JC, Plasse JC, Revol M, Gilly R. Prevention of recurrent febrile convulsions: a randomized therapeutic assay: sodium valproate, phenobarbital and placebo. *Neuropediatrics* 1984;15:37-42.
  134. Minagawa K, Miura H. Phenobarbital, primidone and sodium valproate in the prophylaxis of febrile convulsions. *Brain Dev* 1981;3:385-93.
  135. Newton RW. Randomised controlled trials of phenobarbitone and valproate in febrile convulsions. *Arch Dis Child* 1988;63:1189-91.
  136. Pearce JL, Sharman JR, Forster RM. Phenobarbital in the acute management of febrile convulsions. *Pediatrics* 1977;60(4 Pt 2):569-72.
  137. Vining EP, Mellitis ED, Dorsen MM, et al. Psychologic and behavioral effects of antiepileptic drugs in children: a double-blind comparison between phenobarbital and valproic acid. *Pediatrics* 1987;80:165-74.
  138. 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;59:378-85.
  139. Wolf SM. Prevention of recurrent febrile seizures with continuous drug therapy: efficacy and problems of phenobarbital or phenytoin therapy. In Nelson KB and Ellenberg JH (eds) *Febrile Seizures*. New York, Raven Press 1981:127-134.
- Sodium Valproate
140. Ngwane E, Bower B. Continuous sodium valproate or phenobarbitone in the prevention of 'simple' febrile convulsions. Comparison by a double-blind trial. *Arch Dis Child* 1980;55:171-4.
  141. Wallace SJ, Smith JA. Successful prophylaxis against febrile convulsions with valproic acid or phenobarbitone. *Br Med J* 1980;280:353-4.
- Clobazam / Nitrazepam
142. Manreza ML, Gherpelli JL, Machado-Haertel LR, Pedreira CC, Heise CO, Diament A. Treatment of febrile seizures with intermittent clobazam. *Ar Neuropsiquiatr* 1997;55:757-61.
  143. Tondi M, Carboni F, Deriu A, Manca S, Mastropaolo C. Intermittent therapy with clobazam for simple febrile convulsions. *Dev Med Child Neurol* 1987;29:830-1.
  144. Vanasse M, Masson P, Geoffroy G, Larbrisseau A, David PC. Intermittent treatment of febrile convulsions with nitrazepam. *Can J Neurol Soc* 1984;11:377-9.
- Parental Education
145. Balslev T. Parental reactions to a child's first febrile convulsion. A follow-up investigation. *Acta Paediatr Scand* 1991;80:466-9.
  146. Banco L, Veltri D. Ability of mothers to subjectively assess the presence of fever in their children. *Am J Dis Child* 1984;138:976-8.
  147. Camfield CS, Camfield PR. Febrile seizures: an Rx for parent fears and anxieties. *Contemporary Pediatrics* 1993;10:26-44.
  148. Rosman NP, Colton T, Labazzo J, et al. A controlled trial of diazepam administered during febrile illnesses to prevent recurrence of febrile seizures. *N Engl J Med* 1993;329:79-84.