

Febrile seizures in children

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Abstract

Febrile seizures may be the most common seizure disorder affecting children between the ages of six and 60 months. Febrile seizures may be classified as simple, complex and symptomatic. Simple febrile seizures may last for less than 15 minutes. Possible causes of febrile seizures may include a genetic predisposition, infection and certain vaccines. The management of febrile seizures includes the use of antipyretics, and depending on the duration of the seizure, the use of anticonvulsants. This article deals with the management of febrile seizures in paediatrics. Incorporating the pharmacist as part of the clinical team, and using appropriate educational tools, may assist febrile seizure prognosis.

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Introduction

Febrile seizures are a fairly common seizure disorder in childhood, and are associated with fever, but without any evidence of other intracranial infections or abnormalities.^{1,2} They may be classified into three groups, namely simple, complex and symptomatic febrile.^{1,3} Children who have a genetic predisposition may be more prone to developing febrile seizures. Viruses and bacteria have also been identified as possible causative agents.^{4,5} Some vaccines have been associated with an increased risk in seizure development.⁵

Acute management of febrile seizures includes basic emergency procedures, and the use of anticonvulsants, depending on the severity and duration of the seizure.^{2,6-8} Parents are often anxious about febrile seizures, fearing permanent brain damage. Information regarding the condition and its management may decrease some of this anxiety, and may also ensure proper management of the condition.^{2,7,9} The likelihood of febrile convulsions causing neurological abnormalities or developmental disturbances is low.^{2,6,7,10} Antiepileptic medication may be used to prevent recurrent febrile seizures, e.g. primidone and valproic acid. However, toxicities associated with these drugs outweigh the relatively minor risks associated with febrile seizures.^{1,2} With education and appropriate pharmacological management, simple febrile seizures can be considered to be a benign condition with an excellent prognosis.¹

Definitions

Febrile seizures are defined as seizures occurring between the ages of six and 60 months, in children with fever.^{1,4} These seizures

are not accompanied by intracranial infections or other metabolic disturbances.^{1,4} Febrile seizures may be the most common of all seizure disorders in children, affecting two to five per cent of children between the ages of six and 60 months.¹ Febrile seizures may be classified into three groups (see Table I).^{2,6}

Table I: Epidemiological classification of febrile seizures⁶

Simple	Complex	Symptomatic febrile
Fever in a child aged six to 60 months. Simple generalised seizure lasting less than 15 minutes. Neurologically healthy by all assessments. Fever and seizure is not caused by infections, e.g. meningitis or encephalitis.	Fever in a child aged six to 60 months. Neurologically healthy by all assessments. The seizure is either focal or prolonged, i.e. > 15 minutes, or multiple seizures occur in close succession.	Fever in a child aged six to 60 months. Neurologically healthy by all assessments. The child has a pre-existing neurological abnormality or acute illness.

Simple febrile seizures last for less than 15 minutes, are generalised, and occur once in a 24-hour period without a focal component. Complex febrile seizures are prolonged (> 15 minutes), have a focal component, and occur more than once in 24 hours.

Normal paediatric temperature ranges are summarised in Table II.⁵ Temperature ranges in paediatrics are higher than those in adults, and should be taken into consideration when diagnosing pyrexia.^{4,11} The rate at which the body temperature rises is not a factor implicated in the pathology of febrile seizures. The threshold of convulsive temperature is independent of the

intensity and duration of the heating stimulus and fever.^{4,5,11} Individual differences, e.g. age and maturation, cause variations in the threshold of convulsive temperatures in individuals.^{5,12} This is further modified by changes in water and electrolyte balance, especially hyponatraemia.^{5,12}

Table II: Normal temperature in paediatrics¹¹

Neonates	36.1-37.7°C
Two-year-old child	37.2°C
Twelve-year-old child	37.0°C

Pathophysiology

Possible causes that could increase the risk of febrile seizure development are depicted in Figure 1.

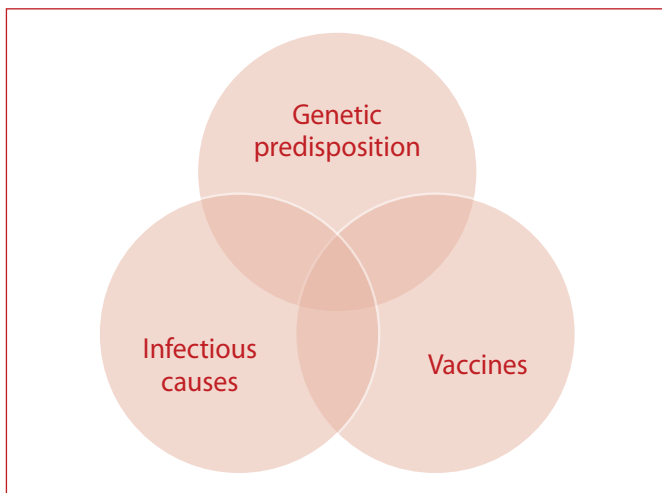


Figure 1: Possible causes of febrile seizures in paediatrics

Febrile seizures occur at a time in childhood when the seizure threshold is low.² This type of epilepsy is unique in that it is always associated with a fever.⁶ Genetic predisposition, with possible polygenic inheritance, has been identified as a cause. An autosomal dominant inheritance pattern, where possible mutations have been found in genes encoding the sodium channel and the gamma amino-butyric acid A receptor A, has been identified in a small number of families.⁴

Febrile seizures can also be classified into three heterogeneous subgroups, based on aetiology and clinical features.⁴

- The largest subgroup comprises children who have seizures in response to fever, and who possess an individual susceptibility that is genetically determined. The children in this subgroup are convulsive in response to fever only. These febrile convulsions are normally referred to as “true” or “pure.”
- A smaller subgroup includes children who are convulsive with fever resulting from an unrecognised brain insult that is due to a febrile condition.

- The third group are children in whom the fever acts as a trigger to elicit true epilepsy, and in whom the convulsions continue to occur, even in an afebrile state.

Children who experience simple febrile seizures may carry the same risk of developing epilepsy by the age of seven years of age as others in the general population (one per cent).¹ The risk increases in children who have had multiple simple febrile seizures at an age of 12 months and younger, and who have a family history of febrile seizures. The risk of these children developing generalised afebrile seizures by the age of 25 increases to 2.4%.¹ There is a possibility that genetic susceptibility to febrile seizures may eventually lead to epilepsy later. The increased risk does not relate to structural brain damage, but rather to genetic predisposition.^{1,4}

An infectious origin may also be a predominant cause of febrile seizures. Viral illnesses have been identified in 2.6% of cases as the cause of fever that leads to a febrile seizure.⁵ Human herpes virus 6 is one of the viruses mostly associated with first-time cases of febrile seizures in children up to two years of age.⁵ Other causes include influenza A virus and respiratory syncytial virus, usually during early spring and winter in annual epidemics.⁵ Viral infections may be complicated by secondary bacterial infections. However, they are found to be lower in febrile children suffering from influenza A or respiratory syncytial virus infections.^{4,5} To reduce the use of unnecessary antibiotics, children presenting with pyrexia should be tested for virus infections.^{4,5}

Mechanisms through which viruses have been postulated to cause febrile seizures include fever, a degree of fever that exceeds the individual threshold for convulsions, and an abnormal immune response to an infection and elevated cytokine levels.⁵

The use of vaccines has also been associated with an increased risk of febrile seizure development.⁵ The measles-mumps-rubella (MMR), measles-rubella and diphtheria-tetanus-pertussis (DTP) vaccines have been associated with an increased risk of febrile seizures during the first three years of life.⁵ The MMR vaccine may cause febrile seizures to occur between seven to 14 days later, whereas the DTP vaccine is known to cause seizures on the day of the vaccination.⁵ Children who experience vaccine-related seizures have an increased risk of recurrent febrile seizures and an associated family history of febrile seizures.⁵

Compared to viral infections, bacteraemia is a less frequent cause of febrile seizures.^{4,5} However, *Streptococcus pneumoniae* has been implicated as a cause of simple febrile seizures by causing bacterial meningitis.^{4,5,13} Meningitis should be ruled out in a child presenting with pyrexia. However, it is very unusual for a child with meningitis to present with a seizure only.^{4,5,13} Other discriminate factors should also be taken into consideration, e.g. the presence of one or more of the major signs, e.g. petechial and nuchal rigidity.^{4,5,13} It has been found that febrile seizures associated with shigellosis are not caused by the toxin of *Shigella dysenteriae*, but rather to the degree of fever and the dehydration associated with the loss of water and electrolytes.⁵

In some studies, the use of prenatal alcohol and cigarette smoking was associated with an increased risk of febrile seizure development.¹⁴⁻¹⁶ In one cohort study, prenatal exposure to low-to-moderate levels of alcohol and coffee was found to have no impact on the risk of febrile seizure development.¹⁷ However, as a risk factor, modest smoking could not be ruled out completely.¹⁷

Management

When managing children with febrile seizures, the fever's origin should be investigated.^{2,6,18} Febrile seizures should be distinguished from "seizures with fever".⁷ The latter includes seizures in any child with a fever for whatever cause.⁷ Conditions such as meningitis, encephalitis, or cerebral malaria, are not febrile seizures, but seizures accompanied by a fever.⁷ Routine diagnosis, using lumbar punctures, is not recommended in children presenting with simple febrile seizures.^{18,19} However, the risk of meningitis is higher in younger children, and further investigation is recommended into children who seem unwell, or who present with altered consciousness.¹⁸ Prophylactic treatment, i.e. the use of antiepileptic agents, is not recommended, and has not proven to reduce the likelihood of future febrile seizures.^{2,3,6,18}

Acute management of febrile seizures

Acute management of febrile seizures includes a number of measures (see Table III).^{2,6-8}

Table III: Acute management measures for febrile seizure treatment		
Measure		✓
1	Airway: Maintain a patent airway	✓
2	Breathing: Ensure effective breathing. Oxygen may be administered, if available.	✓
3	Protect the child from injury: Place in a semi-prone position, and remove any excess or loose clothing.	✓
4	Fever: Treat the fever by sponging with lukewarm water, and administer antipyretics, e.g. paracetamol or ibuprofen	✓
5	Depending on the duration of the seizure, administer the following according to the physician's script: <ul style="list-style-type: none"> • Rectal diazepam if the seizure lasts for more than five minutes; • Intravenous anticonvulsant, i.e. diazepam, lorazepam or phenobarbital, if the patient is still convulsing for longer than 15 minutes. 	✓

Children should be observed for several hours before they are to be discharged.^{2,7} Discharge should only be carried out if the origin of the fever has been established and treated, and if the treating physician deems the child to be clinically stable.^{2,7}

Providing the parents with support

Parents are often anxious, and fear that their child will die, or have permanent brain damage.^{2,7} These needs have to be addressed, and the parents should be reassured.^{2,7}

Upon discharge, the following information should be given to parents:^{7,9,10}

- Most febrile seizures have an excellent prognosis.
- Education on first aid when a seizure has occurred, for example on positioning, i.e. the supine position (by turning the head to face sideways while tilted upward), not attempting to insert anything into the mouth, and not giving any drugs or fluids orally.
- Simple techniques, e.g. how to measure temperature, and how to administer the antipyretic, and how much.
- Following another seizure, the following should be noted: an accurate description of the seizure, including its duration; information about the nature of the seizure; the child's temperature at the time it occurred; and any other signs and symptoms that may have accompanied it.

Prognosis

Most authors agree that the likelihood of febrile convulsions causing neurological abnormalities or developmental disturbances is low.^{2,6,7,10} The risk of developing an intellectual deficit is higher in those who already suffer from a pre-existing neurological or developmental abnormality, or in patients who subsequently develop afebrile seizures.⁷ About one-third of children who experienced a single febrile seizure will suffer another. This ratio may increase to half of patients if the onset is below one year of age.^{7,10}

Children suffering from febrile seizures have a slightly higher risk of developing epilepsy compared to other children (2% vs. 1%).

The risk factors for developing epilepsy are also dependent on pre-existing neurological defects and abnormalities, a family history of afebrile convulsions, and a complex first febrile convulsion.⁷

Prophylaxis of recurrent febrile seizures

There is some evidence that both continuous antiepileptic therapy, with phenobarbital, primidone, or valproic acid, and intermittent therapy, with oral diazepam, are effective in reducing the risk of recurrence of febrile seizures. However, the toxicities associated with these drugs outweigh the relatively minor risks associated with febrile seizures.^{1,2} Phenobarbital depresses cognitive performance in children being treated for febrile seizures, and this side-effect outlasts the drug's administration by several months, and is not offset by the benefit of seizure prevention.²⁰

The use of diazepam may decrease the number of febrile seizures when administered at the onset of fever.^{2,7} Intravenous diazepam

controls seizures more quickly than intranasal midazolam. However, intranasal midazolam may be just as safe and effective as diazepam, and can be administered at home to children suffering from febrile seizures, providing appropriate instructions are given.²¹

Carbamazepine and phenytoin have not proven to be effective in preventing simple febrile seizures. Even when the agents are within the therapeutic range, this may be the case.¹ Evidence that antipyretic treatment prevents the recurrence of febrile seizures remains scarce. The use of an antipyretic agent should be given to provide comfort to the patient, and to prevent dehydration. Adequate fluid intake should be maintained.²² Paracetamol and ibuprofen are the two most common antipyretics used in the management of fever in children, and should be given in paediatric dosages to relieve discomfort secondary to fever.²

Conclusion

Febrile seizures are a common seizure disorder in childhood. Children suffering from febrile seizures should be evaluated to ensure that there are no underlying disorders. Should any be discovered, these should be treated timeously. Prompt diagnosis, and reassuring and educating the parents should help to decrease their anxiety. Pharmacological management should be individualised according to the type of seizure, but also according to the patient's healthcare needs.

References

- Steering Committee on Quality Improvement and Management, Subcommittee on Febrile Seizures American Academy of Pediatrics. Febrile seizures: clinical practice guideline for the long-term management of the child with simple febrile seizures. *Pediatrics*. 2008;121(6):1281-1286.
- Tejani NR. *Pediatrics*, febrile seizures. *emedicine* [homepage on the Internet]. c2010. Available from: <http://emedicine.medscape.com/article/801500-overview>
- Offringa M, Moyer V. Evidence based management of seizures associated with fever. *BMJ*. 2001;323(7321):1111-1114.
- Iwasaki N, Nakayama J, Hamano K, et al. Molecular genetics of febrile seizures. *Epilepsia*. 2002;43(Suppl 9):32-35.
- Millchapp JG, Millchapp JJ. Role of viral infections in the etiology of febrile seizures. *Pediatric Neurology*. 2006;35(3):165-172.
- Bauman R. Febrile seizures. *emedicine* [homepage on the Internet]. c2010. Available from: <http://emedicine.medscape.com/article/1176205-overview>
- Wong V, Ho MHK, Rosman NP, et al. Clinical guideline on management of febrile convulsion. *Hong Kong Journal of Pediatrics*. 2002;7(3):143-151.
- Lahat E, Goldman M, Barr J, et al. Comparison of intranasal midazolam with intravenous diazepam for treating febrile seizures in children: prospective randomised study. *BMJ*. 2002;321(7253):83-86.
- Parmar RC, Sahu DR, Bavdekar RC. Knowledge, attitude and practices of parents of children with febrile convulsion. *Journal of Postgrad Medicine*. 2001;47(1):19-23.
- Fukuyama Y, Seki T, Ohtsuka C, et al. Practical guidelines for physicians in the management of febrile seizures. *Brain and Development*. 1996;18(6):479-484.
- Wong DL, editor. Whaley and Wong's nursing care of infants and children. 5th ed. St Louis: Mosby-Year Book Inc;1995.
- Millchapp JG. Studies in febrile seizures. Height of body temperature as a measure of the febrile seizure threshold. *Pediatrics*. 1959;23(1 Part 1):76-85.
- Golnik A. Pneumococcal meningitis presenting with a simple febrile seizure and negative blood-culture result. 2007;120(2):e428-e431.
- Nelson KB, Ellenberg JH. Prenatal and perinatal antecedents of febrile seizures. *Annals Neurology*. 1990;27(2):127-131.
- Berg AT, Shinnar S, Shapiro ED, et al. Risk factors for a first febrile seizure: a matched case-control study. *Epilepsia*. 1995;36(4):334-341.
- 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(3):462-473.
- Vestergaard M, Wisborg K, Hendriksen TB, et al. Prenatal exposure to cigarettes, alcohol, and coffee and the risk for febrile seizures. *Pediatrics*. 2005;116(5):1089-1094.
- Thomson K, Tey D, Marks M, editors. *Paediatric Handbook*. 8th ed. Oxford: Wiley-Blackwell Publishing; 2009.
- Kimia AA, Capraro AJ, Hummel D, et al. Utility of lumbar puncture for the first simple febrile seizure among children 6 to 18 months of age. *Pediatrics*. 2009;123(1):6-12.
- Farwell JR, Lee JL, Hirtz DG, et al. Phenobarbital for febrile seizures: effects on intelligence and on seizure recurrence. *New Engl J Med*. 1990;322(6):364-369.
- Lahat E, Goldman M, Barr J, Bistrizter T, Berkovitch M. Comparison of intranasal midazolam with intravenous diazepam for treating febrile seizures in children: prospective randomized study. *BMJ*. 2000;321(7253):83-86.
- Millchapp JG. Antipyretics do not prevent febrile convulsions. *AAP Grand Rounds* 2003;10:42-43.