

# Febrile seizure Dr Afshin Fayazi CHILD NEUROLOGIST

#### References

- Nelson textbook of pediatrics 2020 black color Text
- Swaiman's pediatric neurology 2018 red color Text

#### Febrile Seizures

• Febrile seizures are seizures that occur (in children older than 1 month) between the age of 6 and 60 mo with a temperature of 38C (38.3) or higher, that are not the result of central nervous system infection or any metabolic imbalance, and that occur in the absence of a history of prior afebrile seizures.

- Fc are most common between 6 -60 month (6mo- 3 yr)
- Peak between 18 -24 mo
- 90% of seizures ooccure with in first 3 yr
- 6% before 6 mo
- 6% after 3 yr
- Onset after 7 years is uncommon

- 21% experienced seizure before or within 1 hour of the onset of the fever
- 57 % after 1 to 24 hr of fever
- 22%more than 24 hr after the onset of fever

- A simple febrile seizure is a primary generalized, usually tonic-clonic, attack associated with fever, lasting for a maximum of 15 minand not recurrent within a 24-hour period.
- A complex febrile seizure is
- more prolonged (>15 min), (more than 10 or 15 min),
- is focal,
- and/or recurs within 24 hr. (febrile illness)
- Febrile status epilepticus is a febrile seizure lasting
   >30 min

- Between 2% and 5% (2- 4 %) of neurologically healthy infants and children experience at least 1, usually simple, febrile seizure.
- Simple febrile seizures do not have an increased risk of mortality even though they are concerning to the parents.
- Complex febrile seizures may have an approximately 2-fold long-term increase in mortality, as compared to the general population over the subsequent 2 yr, probably secondary to coexisting pathology.

- There are no long-term adverse effects of having ≥1 simple febrile seizures.
- Specifically, recurrent simple febrile seizures do not damage the brain.
- Compared with age-matched controls, patients with febrile seizures do not have any increase in incidence of abnormalities of behavior, scholastic performance, neurocognitive function, or attention.
- Children who develop later epilepsy might experience such difficulties.

- Febrile seizures recur in approximately 30% of those experiencing a first episode,
- in 50% after 2 or more episodes,
- and in 50% of infants <1 yr old at febrile seizure onset.</li>
   Several factors affect recurrence risk

## Factors associated with increased risk of experiencing FC in children

- A History of FC in a first or second degree relative
- A neonatal nursery stay of more than 30 days
- Developmental delay
- Attandance at day care

## RISK FACTORS FOR RECURRENCE OF FEBRILE SEIZURES

#### **MAJOR**

- Age <1 yr</li>
- Duration of fever <24 hr</li>
- Fever 38-39 C

#### **MINOR**

- Family history of febrile seizures
- Family history of epilepsy
- Complex febrile seizure
- Day care
- Male gender
- Lower serum sodium

recurrence rate : no risk factor:12% , 1 risk factor 25-50% , 2 rf 50-59% 3 or more 73-100%

- Although about 15% of children with epilepsy have had febrile seizures,
- only 2-7% of children who experience febrile seizures proceed to develop epilepsy later in life.
- There are several predictors of epilepsy after febrile seizures

## There are several predictors of epilepsy after febrile seizures

<ul> <li>Simple febrile seizure</li> </ul>	1%
<ul> <li>Neurodevelopmental abnormalities</li> </ul>	33%
<ul> <li>Focal complex febrile seizure</li> </ul>	29%
<ul> <li>Family history of epilepsy</li> </ul>	18%
<ul> <li>Fever &lt;1 hr before febrile seizure</li> </ul>	11%
<ul> <li>Complex febrile seizure, any type</li> </ul>	6%
<ul> <li>Recurrent febrile seizures</li> </ul>	4%

## (genetic factors)

#### **Genetic Factors**

 The genetic contribution to incidence of febrile seizures is manifested by a positive family history for febrile seizures. In many families the disorder is inherited as an autosomal dominant trait, and multiple single genes causing the disorder have been identified.

### (genetic factors)

- In most cases the disorder appears polygenic, and the genes predisposing to it remain to be identified.
- Identified single genes include FEB 1, 2, 3, 4, 5, 6, and 7 genes on chromosomes 8q13-q21, 19p13.3, 2q24, 5q14-q15, 6q22-24, 18p11.2, and 21q22.
- Only the function of FEB 2 is known: it is a sodium channel gene, SCN1A.

 Almost any type of epilepsy can be preceded by febrile seizures, and a few epilepsy syndromes typically start with febrile seizures.

#### These are

- generalized epilepsy with febrile seizures plus (GEFS+),
- severe myoclonic epilepsy of infancy (SMEI, also called Dravet syndrome),
- and, in many patients, temporal lobe epilepsy secondary to mesial temporal sclerosis.

### (GEFS+)

- GEFS+ is an autosomal dominant syndrome with a highly variable phenotype.
- Onset is usually in early childhood and remission is usually in mid-childhood.
- It is characterized by multiple febrile seizures and several types of afebrile generalized seizures, including generalized tonic-clonic, absence, myoclonic, atonic, or myoclonic astatic seizures with variable degrees of severity.

- Dravet syndrome is considered to be the most severe of the phenotypic spectrum of febrile seizures plus.
- It constitutes a distinctive separate entity that is one of the most severe forms of epilepsy starting in infancy.
- Its onset is in the 1st yr of life, characterized by febrile and afebrile unilateral clonic seizures recurring every 1 or 2 mo.

- These early seizures are typically induced by fever, but they differ from the usual febrile convulsions in that they are more prolonged, are more frequent, and come in clusters.
- Seizures subsequently start to occur with lower fevers and then without fever.
- During the 2nd yr of life, myoclonus, atypical absences, and partial seizures occur frequently and developmental delay usually follows.

- This syndrome is usually caused by a new mutation, although rarely it is inherited in an autosomal dominant manner.
- The mutated gene is located on 2q24-31 and encodes for SCN1A, the same gene mutated in GEFS+ spectrum.
- However, in Dravet syndrome the mutations lead to loss of function and thus to a more severe phenotype

- The majority of patients who had had prolonged febrile seizures and encephalopathy after vaccination and who had been presumed to have suffered from vaccine encephalopathy (seizures and psychomotor regression occurring after vaccination and presumed to be caused by it) have Dravet syndrome mutations, indicating that their disease is due to the mutation and not secondary to the vaccine.
- This has raised doubts about the very existence of the entity termed vaccine encephalopathy

#### Febrile Seizures work-up

- Each child who presents with a febrile seizure requires a detailed history and
- a thorough general and neurologic examination.
- These are the cornerstones of the evaluation.
- Febrile seizures often occur in the context of otitis media,
- roseola and
- human herpesvirus 6 (HHV6) infection,
- shigella,
- or similar infections, making the evaluation more demanding.

#### Febrile Seizures &LP

- Lumbar puncture is recommended in children <12 mo of age after their first febrile seizure to rule out meningitis.
- It is especially important to consider if the child has received prior antibiotics that would mask the clinical symptoms of the meningitis.
- The presence of an identified source of fever, such as otitis media, does not eliminate the possibility of meningitis.
- Seizures are the major sign of meningitis in 13-15% of children presenting with this disease, and 30-35% of such children have no other meningeal signs.
- it is strongly recommended in infants <1 yr of age because other signs of the infection might not be present.

#### Febrile Seizures &LP

- A child between 12 and 18 mo of age should also be considered for lumbar puncture because the clinical symptoms of meningitis may be subtle in this age group.
- For the well-appearing child after a febrile seizure, the yield of lumbar puncture is very low.

#### Febrile Seizures &LP

• For children >18 mo of age, a lumbar puncture is indicated in the presence of clinical signs and symptoms of meningitis (e.g., neck stiffness, Kernig sign, Brudzinski sign) or if the history and/or physical examination otherwise suggest intracranial infection.



- Electroencephalogram
- If the child is presenting with his or her first simple febrile seizure and is otherwise neurologically healthy, an EEG need not normally be performed as part of the evaluation.
- An EEG would not predict the future recurrence of febrile seizures or epilepsy even if the result is abnormal.

- Electroencephalogram
- Spikes during drowsiness are often seen in children with febrile seizures, particularly those >4 yr old, and these do not predict later epilepsy.
- EEGs performed within 2 wk of a febrile seizure often have nonspecific slowing, usually posteriorly.
- Thus, in many cases, if an EEG is indicated, it is delayed until or repeated after >2 wk have passed.

- EEG should therefore generally be restricted to special cases in which epilepsy is highly suspected, and it should be used to delineate the type of epilepsy rather than to predict its occurrence.
- If an EEG is done, it should be performed for at least 30 min in wakefulness and in sleep according to international guidelines to avoid misinterpretation and drawing of erroneous conclusions.

• At times, if the patient does not recover immediately from a seizure, then EEG can help distinguish between ongoing seizure activity and a prolonged postictal period sometimes termed a nonepileptic twilight state (NETS).

#### Febrile Seizures & blood studies

- Blood studies (serum electrolytes, calcium, phosphorus, magnesium, and complete blood count [CBC]) are not routinely recommended in the work-up of a child with a first simple febrile seizure.
- Blood glucose should be determined only in children with prolonged postictal obtundation or those with poor oral intake (prolonged fasting).

#### Febrile Seizures & blood studies

- Serum electrolyte values may be abnormal in children after a febrile seizure, but this should be suggested by precipitating or predisposing conditions elicited in the history and reflected in abnormalities of the physical examination.
- If clinically indicated (e.g., in a history or physical examination suggesting dehydration) these tests are indicated.

#### Febrile Seizures & neuroimaging

- a CT or MRI is not recommended in evaluating the child after a first simple febrile seizure.
- The work-up of children with complex febrile seizures needs to be individualized.

• This can include EEG and neuroimaging, particularly if the child is neurologically abnormal.

#### Febrile Seizures & neuroimaging

 Patients with febrile status epilepticus have been reported to have swelling of their hippocampus acutely and subsequent long-term hippocampal atrophy.

 These patients may be candidates for neuroimaging, because they may be at risk for later temporal lobe epilepsy.

- In general, antiepileptic therapy, continuous or intermittent, is not recommended for children with one or more simple febrile seizures.
- Parents should be counseled about the relative risks of recurrence of febrile seizures and recurrence of epilepsy, educated on how to handle a seizure acutely, and given emotional support.

- If the seizure lasts for >5 min, then acute treatment with diazepam, lorazepam, or midazolam is needed
- Rectal diazepam is often prescribed to be given at the time of recurrence of febrile seizure lasting >5 min .
- Alternatively, buccal or intranasal midazolam may be used and is often preferred by parents.

- Intravenous benzodiazepines, phenobarbital, phenytoin, or valproate may be needed in the case of febrile status epilepticus.
- If the parents are very anxious concerning their child's seizures, intermittent oral diazepam can be given during febrile illnesses (0.33 mg/kg every 8 hr during fever) to help reduce the risk of seizures in children known to have had febrile seizures with previous illnesses

- Intermittent oral nitrazepam, clobazam, and clonazepam (o.1 mg/kg/day) have also been used.
- Other therapies have included intermittent diazepam prophylaxis (0.5 mg/kg administered as a rectal suppository every 8 hr),
- phenobarbital (4-5 mg/kg/day in 1 or 2 divided doses),
- and valproate (20-30 mg/kg/day in 2 or 3 divided doses).

- Carbamazepin and phenytoin not effective
- Other antiepileptic drugs (AEDs) have not been shown to be effective.

- In the vast majority of cases it is not justified to use these medications owing to the risk of side effects and lack of demonstrated long-term benefits, even if the recurrence rate of febrile seizures is expected to be decreased by these drugs.
- Chronic antiepileptic therapy may be considered for children with a high risk for later epilepsy.

 Antipyretics can decrease the discomfort of the child but do not reduce the risk of having a recurrent febrile seizure, probably because the seizure often occurs as the temperature is rising or falling.

- Currently available data indicate that the possibility of future epilepsy does not change with or without antiepileptic therapy.
- Iron deficiency has been shown to be associated with an increased risk of febrile seizures, and thus screening for that problem and treating it appears appropriate

