SOUTHWEST CHILDREN'S CENTER

# FEBRILE SEIZURES

Febrile seizures, seizures precipitated by fever in young children are a not uncommon disorder affecting an estimated two to five percent of infants and young children. There is some "modest wiggle room" in a lot of the numbers and percentages linked to any conversation regarding febrile seizures as the quoted percentage of children affected by febrile seizures in the first sentence. Many reputable authorities in the field would say that febrile seizures occur between six months and six years of age. Fever associated seizures occurring outside these limits likely represent pathology other than febrile seizures and should be evaluated as probable alternate pathology.

The most common age for onset of febrile seizures is the second year of life. The typical seizure lasts less than five minutes, often only a matter of seconds and is a jerking of both arms and both legs ( a generalized "tonic- clonic" seizure). This is followed by a brief period of sleepiness / lethargy and diminished "tone" before returning to "baseline". Baseline will usually be a sick child because fever is being caused by some sort of illness, so the child is not returning to a state of "wellness". Rather this child is returning to a state of illness. In modern America one half of febrile seizures are caused by HHV-6 and HHV-7, the two closely related human herpes group viruses responsible for the childhood illness roseola. When the post febrile seizure patient returns to baseline, often little or no lab evaluation will be needed in the care of the patient. This is less true for infants below a year of age or toddlers experiencing a series of seizures over time so that the baseline of illness to which they return is difficult for the physician to evaluate. In that circumstance, laboratory testing often including a lumbar puncture to evaluate for spinal fluid infection and central nervous system imaging studies may be needed to assure that the pathology is that of a febrile seizure.

This sort of investigation has dramatically changed over the decades. A mere thirty-five years ago the first vaccine to prevent bacterial meningitis caused by Haemophilus influenza type B was introduced into use in the United States. That vaccine and subsequent improvements in the vaccine virtually eliminated this most common cause of bacterial meningitis among vaccinated infants and children. This changed the care of febrile seizures from mandatory lumbar puncture and IV antibiotics to one that is usually observational and non-invasive. The benefits to children and their families are inestimable even in this exceedingly limited application when discussing the benefits of vaccines.

There is no doubt that the seconds to a few minutes duration of a typical "simple" febrile seizure will seem to be many times longer to the parents who witness such an event in their child. Harrowing though it may be, once the first febrile seizure resolves other questions about future febrile seizures and the risk of eventual epilepsy (recurrent seizures without fever) begin to deserve thought.

Recurrences of febrile seizures are related to risk factors surrounding the first febrile seizure. If there are "complex" features, risk is increased.

1. If the age at the first febrile seizure is < 1 year this child has more years in the febrile seizure age rage, hence increased risk.

2. Most simple febrile seizures occur at the beginning of the fever. If fever is present for more than 24 hours before the febrile seizure, this is a "complex" feature.

3. If the fever that provokes the seizure is minimal (e.g. 101 degrees) versus maximal (e.g. 105 degrees), risk is conferred if the seizure takes place at the lower temperature.

4. If the seizure is focal (only a part of the body is initially involved in the seizure) before it generalizes to the entire body, this is a "complex" feature.

5. If there is more than a single seizure during a single illness, this is a "complex" feature.

6. If the seizure is prolonged and lasts longer than thirty minutes, this condition is referred to as febrile status epilepticus (FSE) and is considered a "complex" feature.

7. Family history of febrile seizures confers risk of recurrence and should be sought from other family members because this sort of family history is not always well known and confers risk if present

8. If the child has neurodevelopment that is not normal, risk is conferred.

If there are two risk factors surrounding the first febrile seizure, recurrence probability is thirty percent. If three or more risk factors, recurrence probability increases to sixty percent. If the initial febrile seizure was a prolonged "FSE", though there is no assurance of recurrence, if there is a recurrence there is heightened risk of a prolonged "FSE". Even so, recurrences are very individualistic and risk probabilities should not be regarded as a certainty.

The risk of future epilepsy is still largely unknown. Again, there is risk stratification based on factors surrounding the febrile seizures. Risk factors include:

1. Family history of epilepsy.

2. Long duration of fever before febrile seizure.

3. "Complex" febrile seizure features as above.

4. Febrile status epilepticus - febrile seizure lasting longer than 30 min.

5. Neurodevelopmental differences

No matter the risk factors associated with febrile seizures, there are no known interventions (use of antiepileptic medications, use of fever medications) that will alter the potential for future epilepsy. The probability of developing epilepsy:

1%: The risk of epilepsy in the general population is one percent.

2%: The risk of epilepsy if there was a simple febrile seizure.

4%: The risk of epilepsy if there are "complex" features.

10%: The risk of epilepsy if there was febrile status epilepticus.

Treatment of simple febrile seizures is largely supportive and once it was believed that the occurrence of a simple febrile seizure is a benign event. This is largely true, but we know a subgroup of patients, especially those with "FSE" can have consequences. Seizures lasting longer than thirty minutes are the

most common neurological emergency in childhood. We know that children with primary FSE have a higher risk for future FSE. For families living a considerable distance from medical intervention or those where first responders cannot administer antiepileptic medications having a rescue plan in place for prehospital administration of antiepileptic medications would be reasonable.

Rectal diazepam (Diastat) has been the only licensed antiepileptic medication for home administration by family members. That landscape is changing in late 2019 with intranasal midazolam and diazepam approved but not yet available. Buccal diazepam is not yet approved, but approval is expected. Clonazepam wafers are available in Europe but are not approved for use in children in the United States. In the not distant future there will be other options increasing the likelihood that families will be increasingly involved in a prehospital rescue plan for children at risk for FSE.

Vaccinations and febrile seizures, FSE, GEFS+, and Dravet's syndrome (see below) have a limited relationship but are worthy of a discussion in any conversation about febrile seizures. We know that children less than two years of age receiving a measles containing vaccine (MMR) are at a modest risk of a febrile seizure. This risk is accentuated if given together with a varicella vaccine in the same syringe. After four years of age, that risk no longer exists. Whole cell DTP vaccine, no longer used in the United States is associated with fever induced seizures while the currently used split cell DtaP vaccine is not associated with seizures. Neither the American Academy of Pediatrics or the World Health Organization recommend avoidance or alteration of the current immunization recommendations out of concern of febrile seizures. This is true even for the considerably more concerning febrile seizure syndromes, GEFS+ and Dravet's syndrome.

Both of these syndromes are the consequence of either inherited or new mutations in either the SCN1a or SCN1b genes that control sodium ion channels. This is new and complex genetic science and in the past would not have had an adequate scientific explanation to promote understanding. Therefore, speculation about the relationship between immunizations and the worst seizure disorders temporally associated with vaccinations, fever, seizures and especially in the case of Dravet's syndrome neurocognitive degeneration is misplaced in light of the evolving science that explains this association. A typical scenario could have been the administration of six months vaccines, resultant fever followed by a prolonged seizure greater than thirty minutes in duration (FSE). Then a series of difficult to control prolonged seizures with associated neurocongnitive degeneration. In the absence of an understanding of the genetic differences that result in the neurological changes, it would be easy to understand why the "blame" for this disorder would have been related to vaccines. The vaccines are not causative, but in some instances would have been the first provocative fever and in these two syndromes seizures are exquisitely fever sensitive initially. The seizures gradually become less fever sensitive and seizures begin to occur without a provocative fever.