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IN THIS ISSUE

Evaluating/Treating Childhood Febrile Seizures

By Karen Richards, MD, Child Neurologist and Epileptologist

Two to 5 percent of children younger than five years will experience a febrile seizure. Because of this high incidence, these events have been well studied, allowing the development of practice parameters recommending a specific approach to evaluation and treatment.

Some physicians feel that practice parameters relegate clinical decision-making to a cookbook approach that encourages regimented evaluation without considering individual patient variables. Viewed differently, practice parameters allow a standardized approach as a starting point to ensure adequate diagnostic evaluation and prevent unnecessary tests, while remaining mindful of each patient's unique concerns in context.

This article discusses the diagnostic approach and treatment options for febrile seizures in light of the practice parameters and highlight situations where individual considerations may require more thought. The practice parameters address only simple febrile seizures. Complex febrile seizures generate more controversy in approach to management, and some of these quandries will be addressed here as well.

Defining Febrile Seizures: The Finer Points

Febrile seizures constitute a diagnostic category that predicts a benign prognosis. To enter this benign diagnostic group, three requirements must be met: age between six months and five years, a fever present at the time of the seizure and absence of a previous neurologic condition. (Refer to the "Diagnostic Features of Simple Vs. Complex Febrile Seizures" table.) Identification of a simple febrile seizure in an otherwise healthy child allows predictions for recurrence, low risk of epilepsy in the future, low risk of comorbid diagnoses and high probability that recurrences will terminate after age five. Children younger or older than this range have a predictably different prognosis and cannot be included under the spectrum of febrile seizures. Likewise, the occurrence of fever during the seizure is objective and relatively easy to ascertain. Although any febrile illness could provoke a seizure in a child with a relatively lower seizure threshold, the occurrence of a seizure without fever during the seizure itself must be viewed differently. One study by Lee and Ong demonstrated that afebrile seizures during intercurrent infections were prognostically more severe than true febriles seizures, but much more benign that unprovoked afebrile seizures. However, these prognostic findings have not been verified to the same degree as in populations of febrile seizures. Without a fever at the time of a seizure, the possibility of a symptomatic seizure, either from the underlying infection, injury or from a structural brain lesion that might lower the seizure threshold, demands consideration for further workup.

Diagnostic Features of Simple Vs. Complex Febrile Seizures

The third criterion (absence of a neurologic condition) is not always cited, but is important to prevent mislabeling seizures in children more likely to have a seizure disorder provoked by a fever, rather than purely benign febrile seizures. The practice parameter excluded studies with patients with previous neurologic conditions, raising the question of what degree of deficit constitutes a pre-existing condition. While a child with cerebral palsy or hydrocephalus would clearly be excluded from a clinical group of febrile seizures, what about isolated speech or motor delay, or autism? These less severe neurologic diagnoses should be kept in mind in evaluating the child and counseling the family.

Diagnostic Features of Simple vs. Complex Febrile Seizures

	Simple Febrile Seizures	Complex Febrile Seizures
Age	**6 months to 5 years**	**6 months to 5 years**
Fever present during seizure	Yes	Yes
Previous neurologic Diagnosis	None	None
Seizure type	Generalized convulsion	Any other type
Focal features	None	Present or absent
Duration	< 15 minutes	> 15 minutes
Recurrence	None within 24 hours	Any number within 24 hours

Given the frequent occurrence of both mild developmental delays and febrile seizures, their co-occurrence would be frequent and therefore the inclusion of such children into a diagnostic group of entirely normal children with febrile seizures is accurate in most cases.

Complex febrile seizures constitute a subgroup (< 12 percent) of children who would otherwise meet diagnostic criteria for febrile seizures. The unfortunate name of this group results in confusion of these categories with the distinction between simple and complex partial seizures. A simple febrile seizure must be a generalized convulsion, brief in duration and not recurrent. Complex febrile seizures manifest as any other type of seizure (limpness, staring, collapse without convulsion), any with focal features (unilateral movement, Todd's paralysis, turning of the head or eyes to one side), any prolonged events (>15 minutes) or recurrence within 24 hours. The significance of these features lies in a higher risk for later development of epilepsy. The distinctive type of seizure may signal an underlying brain lesion or a genetic condition that provokes partial rather than generalized seizures.

AAP Practice Parameter Recommendations for Evaluating First Simple Febrile Seizure

Once an event has been identified as a simple febrile seizure, the practice parameter recommendations apply. Extensive literature review and consensus opinion led to their development. Diagnostic evaluation begins with an evaluation as to the cause of fever. As with any other febrile child, age and height of temperature, history and physical examination all play a role in determining necessary diagnostic tests. Because a seizure has occurred, meningitis, either viral or bacterial, must be considered in the differential diagnosis. The clinical diagnosis of meningitis, or exclusion thereof, is strongly affected by patient age.

Children 6-12 months of age AND any child exposed to antibiotics during their febrile illness may present few obvious clinical signs of meningitis, and lumbar puncture should be strongly considered. Children between 12 to 18 months (not exposed to antibiotics) should be considered for lumbar puncture more intently than children older than 18 months. Up to 35 percent of children with meningitis may lack clinical signs, mostly children less than 18 months of age. Factors that increase the likelihood of abnormal CSF results include: 1) abnormal physical examination (focal neurologic signs, petechiae), 2) complex febrile seizures, 3) physician visits within 48 hours BEFORE the seizure, 4) seizures occurring in the emergency department, 5) prolonged postictal states, and 6) age >three at time of first febrile seizure. Furthermore, the occurrence of a specific source for fever, such as otitis media, does not preclude the possibility of coexistent meningitis.

Aside from evaluation for cause of fever and consideration of lumbar puncture, the practice parameter does NOT recommend any further diagnostic testing. Although blood studies such as CBC, electrolytes and blood glucose are frequently performed, the published evidence does not suggest that these studies contribute to the evaluation of simple febrile seizures. However, these tests may be relevant to the underlying illness, such as chemistries in a dehydrated child or a CBC to assess for sepsis.

Despite the frequent practice of a routine diagnostic head CT, the practice parameters recommend against routine imaging of children with simple febrile seizures. The yield of imaging is low and does not justify the significant radiation exposure recently stressed to be of measurable consequence to young children. However, a focal complex febrile seizure or focal neurologic findings should prompt an imaging study.

The practice parameters do not recommend EEG since the result does not predict the occurrence of future febrile or afebrile seizures (epilepsy). Although the parameters do not provide recommendations for complex febrile seizures, studies that have included patients with complex febrile seizures fail to show a role for EEG in predicting the occurrence of epilepsy.

AAP Practice Parameter Recommendations for Treatment of Simple Febrile Seizures

Again this second practice parameter applies only to neurologically healthy (see comments above) children with simple febrile seizures. Recurrence of febrile seizures is common, occurring in 25-30 percent of children after one simple febrile seizure, 50 percent of children after a second event and 50 percent of children whose first event occurs

before six months of age. According to a study by Annegers et al, having a febrile seizure with complex features does not in itself increase the risk of recurrence, but when occurring in a child younger than 18 months with a family history of febrile seizures, risk of recurrence increases. Shinnar et al reported that low temperature and short duration of fever

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For more information, please contact Karen Richards, MD (pictured above), 'Specially for Children, Pediatric Neurology and Epileptology, at (512) 324-8140. To access patient referral forms online, visit *www childrenshospital.com.*

Coronary Calcium Scoring

Relic of Cardiology or Useful Tool for the Clinician?

By Fotini Chalkias, MD, Cardiologist
with Texas Cardiovascular Consultants

What is a cardiac Calcium score?

A Calcium score, or "heartsaver" score, is a number that reflects the degree of coronary calcification in the coronary arteries. The patient is also given a percentile of calcification compared to other patients of similar age and sex. The presence of calcium in coronary arteries is pathognomonic of atherosclerosis.

How is it obtained?

The score is obtained by doing a noncontrast, low resolution CT of the chest.

How much radiation is involved in obtaining the scan?

The radiation of the scan is equivalent to the baseline radiation obtained by living in Austin in one year (approximately 2 miliSeverts).

How do you use the data?

Mostly, the data is used to screen patients with moderate, intermediate Framingham risk. If a patient is high risk, then their calcium score is not helpful ba prior understanding that the patient is high risk. A calcium score does not add any additional information.

What is moderate/ intermediate risk?

It is a 10-20 percent, 10-year absolute coronary heart disease risk, which includes the metabolic syndrome, multiple risk factors, a single-markedly elevated risk factor, first degree relative with early onset coronary artery disease (<55 in men and <65 in women).

How does the score compare with other known risk factors for determining cardiac risk?

Diabetes increases the mortality relative risk by 2.5-3x.

Smoking increases mortality relative risk by 2x.

HTN increases relative risk by 2x.

A calcium score of 101-400 increases mortality risk 4x.

A calcium score of 401-1000 increases mortality risk 6x.

A calcium score of >1000 increases mortality risk 12x.

EBT has been found to be an independent and incremental risk factor. The relative risks are adjusted for age, history of diabetes, hypertension, elevated cholesterol and being overweight.

TAKE HOME:
Ca scoring is an excellent prognosticator.

What else do you do with the data?

Identify patients who do not need further cardiac evaluation. A score of zero denotes low risk.

What is low risk?

A study including 2,111 patients underwent Ca scoring before invasive angiography. Coronary calcium was present in more than 99 percent of patients with obstructive coronary artery disease.

No calcium was found in eight patients who had blockages. 7/872 men (0.7 percent)

1/383 women (0.02 percent)

Seven of the eight patients were <45 years old, so the negative predictive power was >99 percent.

Coronary calcium scoring has even been used as a screening tool in the ED in a 1999 Mayo Clinic trial. The sensitivity was 100 percent with a calcium score of zero.

The specificity was 63 percent, so the negative predictive value was 100 percent for significant coronary artery disease.

TAKE HOME:
A score of zero purports very low risk.

Can Calcium scoring be used as a management tool for following disease progression?

Yes, for a change of >15 percent in one year the cumulative MI free survival went from 1 to 0.65 at six years follow up. If a less than 15 percent change occurred in one year, the cumulative MI free survival went from 1 to 0.95 at six years.

TAKE HOME:
A greater than 15 percent increase in coronary calcium scoring in one year leads to increased coronary events.

Does the AHA recommend Ca scoring?

Yes, the recommendation is published in Circulation 2005. The current recommendation is to measure the atherosclerosis burden in clinically selected intermediate Framingham risk patients.

Abnormal CT showing calcium in the coronary artery.

Does a high Ca score effect patients behavior?

Yes, Ca scoring has been shown to increase patient compliance. The odds ratio of maintaining statin therapy increased with increasing levels of calcium scores.

The second quartile increased compliance by 2.4x.

The third quartile increased compliance by 4.2x.

The fourth quartile increased patient compliance by 9.3x.

TAKE HOME:
Ca scoring scares patients into taking their medication.

How does Ca scoring compare to CT angiography?

They are two completely different tests. CT angiography involves getting an IV line placed, infusing IV contrast to similar levels used in a cardiac catheterization, and using much higher radiation. All the precautions that are utilized for renal function and iodine containing contrast must be observed. The radiation levels vary based on CT machine, size of the patient and area being visualized. The levels are usually in the 15-25 miliSevert range (compared to 2 miliSeverts for coronary calcium scoring).

Does ethnicity have anything to do with calcium scoring?

A review of 1,000 subjects between the ages of 40-45 found that African Americans were significantly less likely than whites to have coronary calcium despite having a higher prevalence of hypertension, left ventricular hypertrophy and cigarette smoking. A lower likelihood of coronary calcium in African Americans and Hispanics compared to whites has been noted in other series and could not be explained by differences in risk factors.

TAKE HOME:
Use caution interpreting the coronary calcium score in African Americans and Hispanic patients.

What do you do when an asymptomatic patient has an abnormal calcium score?

Many healthcare providers may want to further examine the clinical significance of an increased calcium score. A treadmill test may be warranted in patients with severe or premature calcification to ascertain the presence or absence of high-grade coronary stenoses (scores greater than 75th percentile for age, sex and race).

Radionuclide imaging or exercise echocardiography are alternatives in patients who have abnormal baseline ECGs. Women should always have an imaging study. Of course, pharmacologic stress radionuclide or echocardiography can be performed in those unable to exercise.

In Summary

Coronary calcification is a powerful tool for risk stratification in an intermediate risk population.

Scores of zero most likely do not need further cardiac testing.

Coronary calcium can track progression of disease and stimulate compliance.

Coronary calcium is not the same as CT angiography.

Race does make a difference in calcium scoring-use with caution. Consider stress testing in patients with scores greater than the 75th percentile.

For any questions or appointments, please call (512) 617-1916.

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before the first febrile seizure also increased the recurrence rate.

Years ago, many children were routinely treated with daily phenobarbital to suppress recurrent febrile seizures. While some studies show that phenobarbital can decrease recurrence rate if given daily at therapeutic levels, other studies do not show efficacy, likely reflecting poor compliance. One large study by Farwell et al of children treated with phenobarbital for febrile seizures demonstrated a lasting effect on cognitive performance: the mean IQ of the children in the treatment group was 8.4 points lower than in the placebo group. This difference persisted after the medication was discontinued. Valproic acid has also demonstrated efficacy for preventing recurrence of febrile seizures, but studies of carbamazepine and phenytoin show them to be ineffective. The practice parameter recommends against continuous use of antiepileptic medications for children with recurrent febrile seizures.

However, the anxiety of parents faced with the potential of recurrence carries weight as well. The frequent advice to suppress fever with antipyretic agents has been proven ineffective for both acetaminophen and ibuprofen. The practice parameter does not endorse antipyretic therapy for seizure prophylaxis, although these medications may be useful for comfort.

So what can be offered to a patient with recurrent febrile seizures with good efficacy and minimal risk? A large study by Rosman et al in 1993 demonstrated that oral diazepam given at 0.33 mg/kg every eight hours during febrile illnesses significantly reduced recurrences from 32 percent in the placebo group to 22 percent in the treated group. The Rosman study generated considerable controversy when initially published due to concerns that the sedating effects of diazepam could theoretically mask meningitis. Other studies using lower doses, smaller sample sizes and including non-compliant patients failed to demonstrate efficacy. While the practice parameters do recommend intermittent diazepam in cases with severe parental anxiety, remember that recurrences still occur at a relatively high rate.

One alternative and common intervention was not addressed in the practice parameter. Because no agents are outstandingly effective in preventing recurrence, a more prudent approach may be to offer parents a means of intervention at the time of recurrence. Rectal diazepam gel provides this opportunity in a safe, reliable and efficacious treatment. Patients with prolonged febrile seizure often generate considerable anxiety over recurrence in both parents and healthcare providers. Data from a study by Shinnar et al of recurrence after a first afebrile seizure show that while a prolonged initial seizure does not increase the risk of recurrence, when a seizure does recur in such a patient, the chance that the subsequent seizure will also be prolonged is significantly increased. Extending these findings to include febrile seizures (not necessarily a valid assumption), it seems reasonable to offer rectal diazepam gel in children with an initial prolonged febrile seizure. Intriguing research by Lewis et al seeks to explain the well-known fact that adults with refractory partial epilepsy due to mesial temporal sclerosis have an increased frequency of a history of febrile status epilepticus. Lewis found that MRI scans performed immediately after prolonged febrile seizures have demonstrated acute edema in the hippocampal area, providing a plausible mechanism for this association. The implications of these findings are being studied further, but given the potential for permanent injury, prolonged febrile seizures should be treated promptly.

Prognosis for Future Afebrile Seizures and Epilepsy

Nearly all parents reasonably wonder whether febrile seizures indicate a risk for epilepsy. The background prevalence of epilepsy in the general population ranges from 0.5-1 percent, and is unchanged in children with a single simple febrile seizure. However, the occurrence of multiple febrile seizures when associated with a family history of epilepsy more than doubles that risk to 2.4 percent. Another study by Annegers et al demonstrated that children with complex febrile seizures have a substantially higher rate of epilepsy with the risk increasing multiplicatively in relation to the number of complex features – up to 49 percent when in patients with three complex features. The development of epilepsy in children who have a history of febrile seizures reflects both acquired conditions (as suggested by Lewis et al, above), and genetic predisposition. Generalized epilepsy with febrile seizures plus (GEFS+) is a hereditary epilepsy resulting from a mutation in a sodium channel gene where family members may exhibit febrile seizures, or generalized epilepsy, or both. Other genes implicated in focal forms of epilepsy have also been linked to febrile seizures (Scheffer et al).

Referrals

Simple febrile seizures in most instances can be managed very appropriately by a primary care provider. Complex febrile seizures raise more questions regarding diagnosis and treatment. As discussed above, imaging should be accomplished in patients with focal febrile seizures, and prolonged febrile seizures may increase the risk of recurrent febrile status epilepticus. In these instances, child neurology referral may be helpful to address parental concerns and review the implications in terms of future risk of epilepsy. Unfortunately, evidence does not suggest that any intervention can alter the enhanced risk of future development of epilepsy.

CONTINUING MEDICAL EDUCATION

The following activities are offered throughout the Seton Family of Hospitals.

*Brackenridge Adult Cancer Management Conference
Brackenridge Hospital
9th Floor Conference Room
4th Wednesday, 7 - 8 a.m.

*Brain & Spine Clinical Grand Rounds
Brackenridge Hospital
9th Floor Conference Room
4th Friday, 7 - 8 a.m.
For more information, please contact Lauren Brandt (lbrandt@seton.org or (512) 324-7782)

*Breast Pre-treatment Management Conference
Brackenridge Hospital
9th Floor Conference Room
1st Monday, 12:15 - 1:15 p.m.

*Central Texas Monthly Pulmonary Chest Conference
Seton Medical Center Austin
Front half of McFadden Auditorium
1st Wednesday, Noon - 1 p.m.

Clinical Psychopharmacology and Therapeutics Lecture Series
Seton Shoal Creek Hospital
6th Floor Large Classroom
Wednesdays, 1 - 2:30 p.m.

Internal Medicine Grand Rounds
Brackenridge Hospital
The Annex Classroom
1st and 3rd Thursday, 12:30 - 1:30 p.m.

Neonatal Grand Rounds
Location alternates between Brackenridge/Children's Hospital of Austin and
Seton Medical Center Austin
3rd Tuesday every other month, except in March and July, Noon - 2 p.m.

OB/GYN Grand Rounds
Seton Medical Center Austin
Network Boardroom
3rd Monday every other month,
12:15 - 1:15 p.m.

*Pediatric Cancer Management Conference
Children's Hospital of Austin
Lower Level ABC Conference Room
3rd Tuesday, 12:15 - 1:15 p.m.

*Pediatric Cardiac Conference
Brackenridge Hospital
Emergency Department Conference Room
Every Friday, 7 - 8 a.m.

Pediatric Grand Rounds
Children's Hospital of Austin
Lower Level ABC Conference Room
2nd and 3rd Thursdays, 12:15 - 1:15 p.m.

Psychiatry Grand Rounds
Seton Shoal Creek Hospital
6th Floor Large Classroom
4th and 5th Tuesdays, Noon - 1 pm

Seton Medical Center Grand Rounds
Seton Medical Center Austin
Front half of McFadden Auditorium
Every Thursday, except 2nd Thursday, 7 - 8 a.m.

*Seton Medical Center Adult Cancer Management Conference
Seton Medical Center Austin
Front half of McFadden Auditorium
2nd Thursday, 7 - 8 a.m.

*GYN Cancer Management Conference
Seton Medical Center Austin
Front half of McFadden Auditorium
Quarterly (Jan, Apr, July, Oct), 1st Wednesday, 7 - 8 a.m.

*Seton Northwest Adult Cancer Management Conference
Seton Northwest
Private Dining Room 2
3rd Thursday, 12:15 - 1:15 p.m.

*Stroke Case Conference
Location varies: Brackenridge Hospital – 2 North Conference Room, or Seton Medical Center Austin – Support Services Conference Room
3rd Thursday every other month beginning in February, Noon - 1 p.m.

*Transplant Board Meetings
Seton Medical Center Austin Boardroom
2 Wednesdays/month, date varies, 7 - 8 a.m.

*Trauma Rounds
Brackenridge Hospital
9th Floor Conference Room
Every Thursday, except 3rd Thursday
6:45 - 7:45 a.m.

* Open to all Seton medical staff members, but closed to non-Seton medical staff and all others.

Current listings for each open activity can be found on **DoctorLink at www.doctors.seton.org**, or in the Seton Family of Hospitals Medical Staff Newsletter. For more information, please contact **Casey Harrison at (512) 324-3023.**

Q&As:

Are the programs listed above open to all physicians?
Activities are open to all Seton medical staff. An activity with an asterisk is closed to non-Seton medical staff and all others.

How do I obtain my CME report?
Contact Medical Staff Services at **(512) 324-1000, ext. 14621.**

Is there a fee for CME reports?
There is no fee for members of Seton's Medical Staff. For all others, there is a $25 fee.

Is there a registration fee for the programs listed above?
The activities listed above do not have a fee. The majority of special conferences charge a fee. These conferences can be located on **DoctorLink at www.doctors.seton.org.**

Could I submit topics for an activity or present an activity myself?
Yes. If you are interested in a specific topic, would like to present at one of the activities or for more information regarding application process, please contact the CME office at **(512) 324-3023.**

Get CME Credits for Your Activity

Does Seton participate in Joint Sponsorships?
Yes. Please call (**512) 324-3023** for more information about applying for a Joint Sponsorship activity.

For more information regarding application process, please contact the CME office at (512) 324-3023 or visit DoctorLink at www.doctors.seton.org.