Special Article

Practice parameter: Evaluating a first nonfebrile seizure in children

Report of the Quality Standards Subcommittee of the American Academy of Neurology, the Child Neurology Society, and the American Epilepsy Society

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Article abstract—*Objective:* The Quality Standards Subcommittee of the American Academy of Neurology develops practice parameters as strategies for patient management based on analysis of evidence. For this practice parameter, the authors reviewed available evidence on evaluation of the first nonfebrile seizure in children in order to make practice recommendations based on this available evidence. *Methods:* Multiple searches revealed relevant literature and each article was reviewed, abstracted, and classified. Recommendations were based on a three-tiered scheme of classification of the evidence. *Results:* Routine EEG as part of the diagnostic evaluation was recommended; other studies such as laboratory evaluations and neuroimaging studies were recommended as based on specific clinical circumstances. *Conclusions:* Further studies are needed using large, well-characterized samples and standardized data collection instruments. Collection of data regarding appropriate timing of evaluations would be important.

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The Quality Standards Subcommittee (QSS) of the American Academy of Neurology (AAN) seeks to develop scientifically sound, clinically relevant practice parameters for physicians for diagnostic procedures, treatment modalities, and clinical disorders. Practice parameters are strategies for patient management that might include diagnosis, symptom, treatment, or procedure evaluation. They consist of one or more specific recommendations based on the analysis of evidence.

Every year, an estimated 25,000 to 40,000 US children experience their first nonfebrile seizure, a dramatic and frightening event.[1-4] This practice parameter reviews available evidence concerning the value of diagnostic testing after a first nonfebrile seizure in a child, and provides recommendations based on this evidence. It addresses the evaluation of children age 1 month to 21 years who have experienced a first nonfebrile seizure that cannot be explained by an immediate, obvious provoking cause such as head trauma or intracranial infection. Reports concerning serum laboratory studies, CSF examination, EEG, CT, and MRI are reviewed. This parameter concerns diagnostic evaluation; a subsequent parameter will focus on treatment of the first nonfebrile seizure.

The seizure types covered by this parameter include partial (simple or complex partial, or partial with secondary generalization), generalized tonic-clonic, or tonic seizures. We are specifically not including children diagnosed with epilepsy, defined as two or more seizures without acute provocation. For this reason, myoclonic and atonic seizures are excluded because they typically are not recognized until there have been multiple occurrences. We defined the first seizure using the International League Against Epilepsy (ILAE) criteria to include multiple seizures within 24 hours with recovery of conscious-

ness between seizures.[5] Children with significant head trauma immediately preceding the seizure or those with previously diagnosed CNS infection or tumor or other known acute precipitating causes are excluded. We excluded neonatal seizures (≤28 days), first seizures lasting 30 minutes or more (status epilepticus), and febrile seizures, because these disorders are diagnostically and therapeutically different. The American Academy of Pediatrics has recently published recommendations for evaluation of children with a first simple febrile seizure.[6]

Description of process. An initial MEDLINE literature search was performed for relevant articles published from 1980 to August 1996, using the following key words: epilepsy, seizures, convulsions, magnetic resonance imaging, computed tomography, electroencephalography, blood chemical analysis, neurological examination, and diagnostic errors. Standard search procedures were used, and subheadings were applied as appropriate. In addition, the database provided by *Current Contents* was searched for the most recent 6-month period. These searches produced 279 titles of journal articles in English, and 79 in non-English languages. An updated MEDLINE search was performed in June 1997 and again in November 1998.

Titles and abstracts were reviewed for content regarding first nonfebrile seizures in children and adults. Articles from the searches were identified for review and additional articles from the references in these primary articles were included. Articles were excluded if they contained only data on adults with established epilepsy, but references were reviewed pertaining to adults with first seizures only, to both children and adults with first seizures, and to children with both new and established seizures. Two of the articles published in non-English languages met our criteria and were included. Of the articles reviewed from searches, bibliographies, and committee member suggestions, 66 met the above criteria and were included as references. The age ranges included in the studies were variable, and most pediatric studies included up to age 16 to 19 years. In most reports, results were not broken down according to subsets of age groups.

A new three-tiered scheme of classification of evidence was developed specifically to be used for evaluation of diagnostic studies (Appendix 1). This classification scheme was approved by the QSS of the AAN and differs from one that has been used for the assessment of treatment efficacy studies, which largely pertains to randomized trials.

Each of the selected articles was reviewed, abstracted, and classified by at least two reviewers. Abstracted data included patient numbers, ages and gender, timing of subject selection (prospective, retrospective, or referral), case-finding methods, exclusion criteria, seizure characteristics, neurologic abnormalities prior to or after the seizure, evalua-

tions and results, and recommendations of the authors. Methods of data analysis were also noted.

Goals of immediate evaluation. After stabilization of the child, a physician must determine if a seizure has occurred, and if so, if it is the child's first episode. It is critical to obtain as detailed a history as possible at the time of presentation. The determination that a seizure has occurred is typically based on a detailed history provided by a reliable observer (Appendix 2). A careful history and neurologic examination may allow a diagnosis without need for further evaluation. Children can present with seizure-like symptoms that may not in fact represent actual seizures, but rather breath-holding spells, syncope, gastro–esophageal reflux, pseudoseizures (psychogenic), and other nonepileptic events. No single clinical symptom can reliably discriminate between a seizure and a nonepileptic event.[7,8] Studies have investigated whether serum prolactin levels[9,10] or creatine kinase levels[11] may help distinguish seizures from nonepileptic events, but neither of these tests is sufficiently reliable to use routinely.

The next goal of assessment is to determine the cause of the seizure. In many children, the history and physical examination alone will provide adequate information regarding probable cause of the seizure[12] or the need for other tests including neuroimaging.[13] The etiology of the seizure may necessitate prompt treatment or provide important prognostic information. Provoked seizures are the result of an acute condition such as hypoglycemia, toxic ingestion, intracranial infection, trauma, or other precipitating factors. Unprovoked seizures occur in the absence of such factors; their etiology may be cryptogenic (no known cause), remote symptomatic (pre-existing brain abnormality or insult), or idiopathic (genetic).

Laboratory studies. *Evidence.* In one Class I study of 30 children ages 0 to 18 years, and 133 adults with seizures, of whom 24 (15%) had new onset seizures, the standard diagnostic laboratory workup, which included complete blood count (CBC), serum electrolytes, blood urea nitrogen (BUN), creatinine, glucose, calcium, and magnesium, revealed one case of hyperglycemia that was unsuspected clinically[14] (95% CI 0, 4.9%). This patient's age was not noted, nor were those with new onset seizures identified by age. Another prospective study of 136 new onset seizure patients found no clinically significant laboratory abnormalities in the 16 children in the study who were ages 12 to 19 years[15] (95% CI 0, 19%).

In two Class II studies including 507 children with both febrile and nonfebrile seizures, results of laboratory studies did not contribute to diagnosis or management.[12,16] In another Class II study including 65 children with new onset seizures not accompanied by fever, one had a positive cocaine screen, and seven had electrolyte abnormalities (additional data supplied by the author of reference 17). Of these, four children were hyponatremic and three were hy-

pocalcemic. Of the four children with hyponatremia, three had a history of illness, lethargy, or diarrhea, and one had no specific symptoms. Of the three with hypocalcemia, one (age 4 months) had clinical signs of rickets, one (age 1 month) had multiple seizures, and one (age 5 years) had a prolonged focal seizure. An exception to the small number of abnormal laboratory findings in the absence of specific suggestive features is in the under 6 month age group. Hyponatremia (<125 mM/L) was found to be associated with seizures in 70% of 47 infants younger than 6 months in a Class II study.[18]

In a sample of 56 children with a first seizure, 40 of whom were febrile, there was one positive urine toxicology screen of the 11 performed. None of 53 hematology tests (95% CI 0, 6%) and two of 96 (2%) chemistry tests were found to be clinically significant (both hyponatremia) (95% CI 0, 11%).[19] In three studies that included a total of 400 adults,[19-21] only 27 (<7%) were found to have abnormalities of calcium, sodium, glucose, BUN, or arterial blood gas (ABG) determinations. Of these abnormalities, only three were unsuspected on a clinical basis.

Conclusions. The fact that a first nonfebrile seizure occurred in the absence of any suggestive history or symptoms in a child who is older than age 6 months and has returned to baseline has not been shown to be sufficient reason to perform routine laboratory testing in the child with a first nonfebrile seizure. However, the number of children reported is too small to be confident that in rare circumstances, routine laboratory screening such as blood glucose determination[12,15,16] might not provide important information, even without specific clinical indications. There were only two reports of positive toxicology screens, but no studies that systematically evaluated the yield from doing routine toxicology screening in children with first seizures. If no cause for the seizure has been identified, it is important to ask questions regarding possible toxic ingestions or exposures.[20]

Recommendations.

- Laboratory tests should be ordered based on individual clinical circumstances that include suggestive historic or clinical findings such as vomiting, diarrhea, dehydration, or failure to return to baseline alertness.[12,14,15,20] **(Option)**

- Toxicology screening should be considered across the entire pediatric age range if there is any question of drug exposure or substance abuse. **(Option)**

Lumbar puncture. *Evidence.* Lumbar puncture (LP) is frequently performed in children in the presence of fever and seizures to rule out CNS infection.[6,21,22] In the only report found giving the frequency of positive spinal fluid examinations in children with nonfebrile seizures, of 57 spinal fluid samples in children ages 2 to 24 months following nonfebrile seizures, 12.3% had >5 leukocytes/mm^{3} in the CSF.[23] These children did not have CNS infec-

tion. CSF glucose increased with seizure duration and the range of CSF glucose was 32 to 130 mg/dL; the range of CSF protein was 9 to 115 mg/dL.[23] A 1993 AAN practice parameter regarding the value of LP did not mention nonfebrile seizure as an indication for LP in either children or adults.[21]

Conclusions. There is no evidence regarding the yield of routine LP following a first nonfebrile seizure. The one study available (Class II) is limited in size and age range. Recommendations based on age and clinical symptoms are available from Class III publications. In the very young child (<6 months), in the child of any age with persistent (cause unknown) alteration of mental status or failure to return to baseline, or in any child with meningeal signs, LP should be performed.[6,21,22] If increased intracranial pressure is suspected, the LP should be preceded by an imaging study of the head.[20]

Recommendations.

- In the child with a first nonfebrile seizure, LP is of limited value and should be used primarily when there is concern about possible meningitis or encephalitis. **(Option)**

EEG. *Evidence.* Of 10 Class I studies reviewed[24-34] (references 26 and 27 were from the same study) and one meta analysis,[35] five studies addressed the prognostic value of EEG in a population of children with a first seizure.[25-27,30,32,33] In four of these studies, epileptiform discharges or focal slowing on the EEG were predictive of recurrence.[25,27,32,33] In children with a cryptogenic (cause unknown) first seizure, 54% of 103 children with an abnormal EEG had a recurrence compared with 25% of 165 children with a normal EEG ($p < 0.001$).[27] EEG abnormalities were reported to be the best predictors of recurrence in children who were neurologically normal; however, abnormal neurologic examination[25,26] and etiology[26,36] were also strong predictors of recurrence. Several of these studies indicated that the information provided by the EEG is useful for diagnosis of the event, identification of a specific syndrome, and prediction of long-term outcome.[26,27,32,33]

Of the four Class I studies of first seizures in adults only, or in both children and adults, an abnormal EEG was predictive for recurrence risk in three studies.[28,29,34] Inclusion of both an awake and a sleep tracing, as well as hyperventilation and photic stimulation,[27,31,32,37-39] are recommended by the American EEG Society,[38] as they increase the yield of abnormalities seen on EEG tracings.

A Class I study published in 1998 in children and adults concluded that an EEG obtained within 24 hours of a seizure was more likely to contain epileptiform abnormalities than one done later (51% versus 34%).[34] The value of an EEG performed in the emergency department shortly after a seizure was addressed in two Class II studies of adult first sei-

zure patients.[40,41] In these studies, interpretation was difficult in the presence of diffuse postictal slowing,[42] and an EEG done at that time was not helpful in determining which patients should be admitted to the hospital.[40]

A recent analysis of selected findings from several of the Class I studies referred to above[25-27,30,31] concluded that an EEG should not be routinely performed after a first seizure because it does not yield sufficient information to alter treatment decisions.[43] To reach this conclusion, the authors did not consider evidence that the EEG result does in fact alter treatment decisions. They assumed a treatment threshold to be at an 80% risk of recurrence, and used a univariate analysis. However, where the EEG is used as one of several variables, it can identify children with very high and very low recurrence risks.[25,26,32,35] The EEG is not used solely to determine recurrence, but also helps differentiate a seizure from other events, is essential to the diagnosis of a syndrome, and provides information on long-term prognosis; it influences the decision to perform subsequent neuroimaging studies[44] and may influence counseling about management of the child.

Conclusions. The majority of evidence from Class I and Class II studies confirms that an EEG helps in determination of seizure type, epilepsy syndrome, and risk for recurrence, and therefore may affect further management decisions. Experts commonly recommend that an EEG be performed after all first nonfebrile seizures.[39,45-47] It is not clear what the optimal timing should be for obtaining an EEG. Although an EEG done within 24 hours of the seizure is most likely to show abnormalities,[34] physicians should be aware that some abnormalities such as postictal slowing that can be seen on EEG done within 24 to 48 hours of a seizure may be transient and must be interpreted with caution.

There is no evidence that the EEG must be done before discharge from the emergency department; the study may be arranged on an outpatient basis. Epileptiform EEG abnormalities may be useful in confirming that the event was a seizure; however, an EEG abnormality by itself is not sufficient to make a diagnosis that an epileptic seizure occurred, nor can its absence rule out a seizure.[46,47] The EEG is necessary to determine the epilepsy syndrome and the diagnosis of an epilepsy syndrome may be helpful in determining the need for imaging studies.[34] The EEG is also useful in predicting the prognosis for recurrences.[20,39,45-47]

It is not clear what the optimal timing should be for obtaining an EEG. Although an EEG done within 24 hours of the seizure is most likely to show abnormalities, physicians should be aware that some abnormalities such as postictal slowing that can be seen on EEG done within 24 to 48 hours of a seizure may be transient and must be interpreted with caution.

Recommendations.

- The EEG is recommended as part of the neurodiagnostic evaluation of the child with an apparent first unprovoked seizure. **(Standard)**

Neuroimaging studies. *Evidence—CT scans.* There were five Class I studies regarding imaging by CT scan after a first seizure; the data pertained to children[32] and adults[24,42,48] with first seizures, and to adults and children over age 6 with both new onset and established seizures.[14] In the single Class I study of first seizures in children, the abnormalities (mostly atrophy) found in 12 children were "without therapeutic consequences" (95% CI 0, 3%).[32] In one of the adult studies, 1.3% of the patients who had CT scans were diagnosed with tumors,[24] and in another, of 62 patients there were three tumors seen on CT, all in patients with abnormal neurologic examinations.[42] Of 119 adults who had CT scans after a first generalized seizure, 20 had abnormalities that warranted therapeutic intervention.[48] In the Class I study in which 19 CT scans were done in selective cases (first seizures if greater than age 6 years, head trauma, or focal seizure), there was one significant abnormality (age of the patient was not given), a subdural hematoma, not predicted by history and physical examination.[14]

Of the 14 Class II studies, nine involved children only (n = 2559),[17,19,49-56] four were of adults only (n = 666),[24,42,57,58] and one involved children and adults (n = 109).[59] Only a small percentage of children in these studies (0 to 7%) had lesions on CT that altered or influenced management. These were most commonly brain tumors, communicating or obstructive hydrocephalus, one subarachnoid and one porencephalic cyst, and three children with cysticercosis. The yield of abnormality on CT when the neurologic examination and EEG were normal was 5 to 10%.[50,54] In a Class II study in which seven children (14% of children with nonfebrile seizures) had CT scans that influenced management, five had focal or complex partial seizures. Abnormalities on neuroimaging were associated with a higher recurrence risk.[54] In one study of febrile and nonfebrile children, CT scans were always normal in the absence of defined risk factors such as known neurologic diagnosis, age <5 months, or focal deficit.[57] Focal lesions on CT scans tended to be more commonly found in adults (18 to 34%)[40,48,57,58] than in children (0 to 12%),[17,32,49,52,54-56] particularly when ordered for specific clinical indications. At least three studies provided evidence that MRI scanning was preferable to CT[51,54,60] in children following nonfebrile seizures.

Evidence—MRI. There was one Class I report regarding MRI in children presenting with a first seizure[54] and another Class I report of newly diagnosed epilepsy in children.[60] Of 411 children who presented with a first seizure, 218 had neuroimaging studies. Four had lesions seen on MRI or CT (two brain tumors, two neurocysticercosis) that potentially altered

Table *Class I and II neuroimaging studies in children*

Reference	No. children	Ages	Class	Method	No. imaged	No. abnormal (%)	95% CI (%)	No. significantly abnormal* (%)	95% CI (%)
Stroink et al., 1998[32]	156	1 mo to 16 y	I	CT	112	12 (11)	9–12	0	0–3
Berg et al., 1999[60]†	273	1 mo to 15 y	I	MRI/CT	236	27 (11)	10–13	0	0–1
King et al., 1998[34]†	59	5 to 16 y	I	MRI	43	3 (3.9)	0–2	0	0–7
O'Dell et al., 1997[54]	411	1 mo to 19 y	I	MRI/CT	218	44 (20)	18–22	4 (2)	2–2
Gibbs et al., 1993[49]	964	2 mo to 17 y	II	CT	121	26 (21)	18–24	2 (2)	1–2
Yang et al., 1979[50]	256	0 to 18 y	II	CT	256	84 (33)	30–36	7 (3)	2–3
McAbee et al., 1989[52]	81	1 mo to 18 y	II	CT	81	6 (7)	6–9	4 (5)	4–6
Warden et al., 1997[56]	158	Median 3.1 y	II	CT	158	10 (6)	5–7	0	0–2
Garvey et al., 1998[17]	65	2 wk to 16 y	II	CT	65	11 (17)	16–24	7 (11)	11–17
Total	2423				1290	223 (17.3)	15–19	24 (1.9)	1–3

* Influencing treatment or management decisions.

† The author provided data regarding analyses of the children who presented with a first nonfebrile seizure.

management.[54] When these four were excluded, 407 children remained in this Class I study. Of these, 58 children had an MRI scan, and 19 (33%) scans were abnormal, but none of the children required intervention on the basis of the neuroimaging findings. In the Class I study of 613 children with newly diagnosed epilepsy, 273 had partial, generalized tonic clonic, or generalized tonic seizures and came to medical attention at the time of their first unprovoked seizure[60] (additional data supplied by the author of reference 60). Of these, 86% had neuroimaging, and none had abnormalities influencing immediate treatment or management decisions. One Class I study of 300 adults and children with first seizures reported 43 MRI scans done in 59 children, one showing hippocampal sclerosis and two showing single gray matter heterotopic nodules (additional data supplied by the author of reference 34).[34] All patients with generalized epilepsy had normal MRI scans.[34] In two Class II reports of retrospective evaluations of MRI in children with seizures, one of which was limited to children with first seizures only, abnormalities on MRI scan such as localized atrophy, mesial temporal sclerosis, and brain malformation were common but did not mandate a change in management.[51,61] There were also six Class III reports.[39,46,62-65]

It was consistently reported in the literature cited above that the MRI was more sensitive than the CT scan.[39,51,54,60,62,63,65] MRI findings included atrophy, infarction, evidence of trauma, cerebral dysgenesis, and cortical dysplasia. Authors of review articles also emphasized a preference for MRI to exclude progressive lesions such as tumors and vascular malformations, or focal cortical dysplasia.[39,62,63,65,66] Neuroimaging was recommended if there is a postictal focal deficit not promptly resolving.[46,66] A recently published practice parameter on neuroimaging in the emergency patient presenting with seizures reviewed literature primarily from adults but included children. This parameter recommended "emergent" neuroimaging if there was suspicion of a serious structural lesion, and that "urgent" neuroimaging should be considered if there was no clear cause of the seizure. This parameter states that if an emergent imaging study is needed, it would be to detect hemorrhage, brain swelling, or mass effect, conditions that are typically adequately imaged on CT.[66] These recommendations were not restricted to any age bracket.

Conclusions. Although abnormalities on neuroimaging are seen in up to one third of children with a first seizure, most of these abnormalities do not influence treatment or management decisions such as the need for hospitalization or further studies (table). Of available reported imaging results, from Class I and Class II studies of children, an average of about 2% revealed clinically significant findings that contributed to further clinical management, the majority of which were performed because the seizure was focal or there were specific clinical findings beyond the fact that a seizure had occurred (see the table).

Thus, there is insufficient evidence to support a recommendation at the level of standard or guideline for the use of routine neuroimaging, i.e., imaging performed for which having had a seizure is the sole indication, after a first nonfebrile seizure in children. However, neuroimaging may be indicated under some circumstances either as an emergent or nonurgent procedure.

The purpose of performing an *emergent* neuroimaging study in the context of a child's first seizure is to detect a serious condition that may require immediate intervention. The possible effects of emergency medication used to treat the seizure must be taken into consideration.

The purpose of performing a *nonurgent* neuroimaging study, which can be deferred to the next several days or later, is to detect abnormalities that may affect prognosis and therefore have an impact

on long-term treatment and management.[20,22] Factors to be considered include the age of the child, the need for sedation to perform the study, the EEG results, a history of head trauma, and other clinical circumstances such as a family history of epilepsy.

Recommendations.

- If a neuroimaging study is obtained, MRI is the preferred modality.[50,51,54,60,62,63,65] **(Guideline)**

Emergent neuroimaging should be performed in a child of any age who exhibits a postictal focal deficit (Todd's paresis) not quickly resolving, or who has not returned to baseline within several hours after the seizure.[46,66] **(Option)**

- Nonurgent imaging studies with MRI should be seriously considered in any child with a significant cognitive or motor impairment of unknown etiology, unexplained abnormalities on neurologic examination, a seizure of partial (focal) onset with or without secondary generalization, an EEG that does not represent a benign partial epilepsy of childhood or primary generalized epilepsy, or in children under 1 year of age.[20,34] **(Option)**

Summary. In the child with a first nonfebrile seizure, diagnostic evaluations influence therapeutic decisions, how families are counseled, and the need for hospital admission and/or specific follow-up plans. This practice parameter has reviewed the published literature concerning the usefulness of studies following a first nonfebrile seizure in children, and has classified the strength of the available evidence. There is sufficient Class I evidence, which involves a well executed prospective study, to provide a recommendation with the highest degree of clinical certainty—i.e., a **Standard**—that an EEG be obtained in all children in whom a nonfebrile seizure has been diagnosed, to predict the risk of recurrence and to classify the seizure type and epilepsy syndrome. The decision to perform other studies, including LP, laboratory tests, and neuroimaging, for the purpose of determining the cause of the seizure and detecting potentially treatable abnormalities, will depend on the age of the patient and the specific clinical circumstances. Children of different ages may require different management strategies.[20,22]

Future research. For most of the questions addressed by this parameter, evidence was insufficient for making a strong recommendation for a standard or guideline, particularly for laboratory studies. In order to generate definitive evidence regarding the value of routine (or selective) laboratory testing and the use of routine neuroimaging studies, sufficiently large samples allowing for adequate statistical power to provide precise estimates (i.e., with narrow confidence intervals) are needed. Neuroimaging studies are needed to understand the significance of neuronal migration defects in the context of a first seizure, and are important because of the improved technical ability of current MRI. In addition, prospective collection of data using standardized treatment protocols and standardized data collection instruments is essential. Results of studies will only be helpful if the patient sample and factors that resulted in inclusion into or exclusion from the sample are well described and documented. Ideally, large consecutive series of well-characterized patients are needed for the results to be accurate and generalizable. Finally, future studies should present separate data from children and adults, and it would be optimal for results in children to be presented by age groupings.

Appropriate timing as well as the choice of evaluative studies have not been adequately studied. Children may present as actively having a seizure when brought to the emergency department, as postictal, or as alert with a history of a possible seizure episode having occurred hours, days, or weeks previously. Data regarding the appropriate timing of laboratory testing, neuroimaging, or EEG studies require adequate prospective studies of these specific questions, with clearly defined entry criteria and a common protocol for type and timing of evaluations.

Research studies with adequate sample sizes and appropriate protocols that provide answers to these questions may serve to reduce the expense and discomfort of unnecessary testing in children with first seizures, and, more importantly, by identifying appropriate candidates, may improve the care and management that these children receive.

Disclaimer. This statement is provided as an educational service of the American Academy of Neurology. It is based on an assessment of current scientific and clinical information. It is not intended to include all possible proper methods of care for a particular neurologic problem or all legitimate criteria for choosing to use a specific procedure. Neither is it intended to exclude any reasonable alternative methodologies. The AAN recognizes that specific patient care decisions are the prerogative of the patient and the physician caring for the patient, based on all of the circumstances involved.

Appendix 1
Classification of evidence
Class I. Must have all of a–d:
a. Prospective study of a well defined cohort which includes a description of the nature of the population, the inclusion/exclusion criteria, demographic characteristics such as age and sex, and seizure type.
b. The sample size must be adequate with enough statistical power to justify a conclusion or for identification of subgroups for whom testing does or does not yield significant information.
c. The interpretation of evaluations performed must be done blinded to outcome.
d. There must be a satisfactory description of the technology used for evaluations (e.g., EEG, MRI).

Class II. Must have a or b:

a. A retrospective study of a well-defined cohort which otherwise meets criteria for Class 1a, 1b, and 1d.

b. A prospective or retrospective study which lacks any of the following: adequate sample size, adequate methodology, a description of inclusion/exclusion criteria, and information such as age, sex, and characteristics of the seizure.

Class III. Must have a or b:

a. A small cohort or case report.

b. Relevant expert opinion, consensus, or survey.

A cost-benefit analysis or a meta-analysis may be Class I, II, or III, depending on the strength of the data upon which the analysis is based.

Appendix 2

Outline for seizure assessment

Features of a seizure:

Associated factors
Age
Family history
Developmental status
Behavior
Health at seizure onset
Precipitating events other than illness—trauma, toxins
Health at seizure onset—febrile, ill, exposed to illness, complaints of not feeling well, sleep deprived

Symptoms during seizure (ictal)
Aura: Subjective sensations
Behavior: Mood or behavioral changes before the seizure
Preictal symptoms: Described by patient or witnessed
Vocal: Cry or gasp, slurring of words, garbled speech
Motor: Head or eye turning, eye deviation, posturing, jerking (rhythmic), stiffening, automatisms (purposeless repetitive movements such as picking at clothing, lip smacking); generalized or focal movements
Respiration: Change in breathing pattern, cessation of breathing, cyanosis
Autonomic: Pupillary dilatation, drooling, change in respiratory or heart rate, incontinence, pallor, vomiting
Loss of consciousness or inability to understand or speak

Symptoms following seizure (postictal)
Amnesia for events
Confusion
Lethargy
Sleepiness
Headaches and muscle aches
Transient focal weakness (Todd's paresis)
Nausea or vomiting

Appendix 3

Strength of recommendations

Standards. Generally accepted principles for patient management that reflect a high degree of clinical certainty (i.e., based on Class I evidence or, when circumstances preclude randomized clinical trials, overwhelming evidence from Class II evidence that directly addresses the issue, decision analysis that directly addresses the issue, or strong consensus of Class III evidence).

Guidelines. Recommendations for patient management that may identify a particular strategy or range of management strategies and that reflect moderate clinical certainty (i.e., based on Class II evidence that directly addresses the issue, decision analysis that directly addresses the issue, or strong consensus of Class III evidence).

Practice options. Other strategies for patient management for which the clinical utility is uncertain (i.e., based on inconclusive or conflicting evidence or opinion).

Practice parameters. Results, in the form of one or more specific recommendations, from a scientifically based analysis of a specific clinical problem.

Appendix 4

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