

## Current Literature

In Clinical Science



## Status Epilepticus Presenting as New-Onset Seizures in Children

### Prospective Study of New-Onset Seizures Presenting as Status Epilepticus in Childhood.

Singh RK, Stephens S, Berl MM, Chang T, Brown K, Vezina LG, Gaillard WD. *Neurology* 2010;74:636–642.

**OBJECTIVE:** To characterize children with new-onset seizures presenting as status epilepticus at a tertiary care children's hospital. **METHODS:** Prospectively collected data were reviewed from a database derived from a mandated critical care pathway. A total of 1,382 patients presented with new-onset seizures between 2001 and 2007. **RESULTS:** A total of 144 patients presented in status epilepticus. The average age was 3.4 years. The majority of seizures (72%) lasted between 21 and 60 minutes. The majority of patients had no significant past medical history; one-fourth had a family history of epilepsy. Five (4%) patients with EEGs had electrographic seizures during the study, captured only with prolonged monitoring. The most common etiology was febrile convulsion, followed by cryptogenic. The most common acute symptomatic cause was CNS infection; the most common remote symptomatic cause was cerebral dysgenesis. Combined CT and MRI provided a diagnosis in 30%. CT was helpful in identifying acute vascular lesions and acute edema, whereas MRI was superior in identifying subtle abnormalities and remote symptomatic etiologies such as dysplasia and mesial temporal sclerosis. **CONCLUSIONS:** Children who present in status epilepticus that is not a prolonged febrile convulsion should undergo neuroimaging in the initial evaluation. For any child who presents in status epilepticus and has not yet returned to baseline, the possibility of nonconvulsive status epilepticus should be considered. Although CT is often more widely accepted, especially in the urgent setting, strong consideration for MRI should be given when available, due to the superior yield.

### Commentary

Status epilepticus (SE), whether in a child or adult, convulsive or nonconvulsive is considered a life-threatening emergency that requires prompt evaluation and treatment. There are several critical issues in accomplishing the former, so that the latter may be pursued. The first is the identification of the condition, status epilepticus. Although it would seem that this should be straightforward, the diagnosis of SE, particularly in the setting of a new-onset seizure can be challenging. The answer to the crucial question “when did this begin” is frequently not known with precision. Unless the family happens to look at a watch or clock, the time of onset may not be known accurately. In addition, children can be found seizing by a parent who hears something unusual or is just checking their child at night. Whether the real duration of the seizure is known or just estimated, the next challenge is to define when the event becomes SE. The duration suggested by the International League Against Epilepsy guideline (1) has been 30 minutes. This duration was selected based primarily on animal studies indicating that this is the critical time after which neurologic damage occurs. However, more recent literature questions the wisdom of putting off more aggressive diagnostic and thera-

peutic measures for that time. A landmark study in adults with refractory generalized tonic-clonic seizures (GTCS) indicated that the mean duration was 62 seconds (with the longest lasting 108 seconds), prompting the authors to suggest that intravenous intervention should be initiated if seizures last more than 2 minutes (2). This and other reports led to the suggestion in 1999 that convulsive SE should be defined as those seizures lasting 5 or more minutes (3). It was acknowledged that the biology and clinical phenomenology of GTCS in children may differ from that of adults. The differences between the child and adult, as well as between new-onset and refractory epilepsy were demonstrated in a prospective study of 407 children with new-onset seizures (4). The investigators used rigorous, standardized interviews in addition to medical record review to determine the duration of these first seizures in children ages 1 month to 19 years. The findings suggested there are two populations of children with regard to seizure duration. One group, which accounted for 76% of patients, had a mean seizure duration of 3.6 minutes, whereas the remaining 24% had a mean seizure duration of 31 minutes! Furthermore, they demonstrated that after 10 minutes, seizures are unlikely to stop spontaneously. Thus, it appears that a small, but significant, population of children have first seizures that raise the specter of SE, with durations commonly greater than 10 minutes. The issue of duration was examined in a study that compared outcomes in individuals with SE ( $\geq 30$  minutes; 91 children and 135 adults) compared with a “prolonged seizure

Epilepsy Currents, Vol. 11, No. 4 (July/August) 2011 pp. 112–113  
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group" (lasting 10 to 29 minutes) consisting of 31 children and 50 adults (5). It was found that almost 43% of the prolonged seizure group stopped spontaneously, whereas the remainder required antiepileptic drug (AED) therapy. If a duration of 5 to 10 minutes was used as the definition of SE, a significant number of patients would have received unnecessary evaluation and treatment.

A relatively recent evidence-based review provided guidelines for the evaluation of SE in children (6). As none of the studies considered were better than Class III, the recommendations were limited to level C ("possibly effective, ineffective or harmful") at best. Thus, the indications for metabolic, toxicologic, hematologic, blood cultures, lumbar puncture, electroencephalography, and neuroimaging were dependent on the individual clinical situations. The recent study by Singh et al. (7) helps further define the etiologies and demographics of SE in children and also provides valuable insight into the utility of diagnostic modalities. The study used prospective data collection as part of a new-onset seizure clinical care pathway in a large children's hospital that serves a wide variety of socioeconomic groups. SE was defined as greater than 20 minutes of convulsive seizures. Approximately 10% of the new-onset population had SE as their first seizure, and 62% did not have a medical or neurologic history that would predispose to seizures. Nonetheless, 28% of this relatively well population had SE that persisted for greater than 60 minutes. The distribution of etiologies was described in categories that made it possible to compare findings with previous studies; revealing that 32% were due to fever, with the next largest etiologies including CNS infection (9%), cerebral dysgenesis (5.6%), and inborn errors of metabolism (5.6%). Thus, the practitioner must be mindful of a broad differential diagnosis that needs to be informed by history as well as laboratory testing. Key findings of diagnostic evaluation include the following: four patients in nonconvulsive SE were discovered by prolonged video-EEG, not by a routine studies; and CT or MRI combined (performed in 97% of patients) revealed abnormalities in 30% of children and influenced care in 24%. MRI revealed metabolic, vascular, dysgenetic, and mesial temporal sclerosis not detected with head CT. Electrolytes had very limited yield (hyponatremia in two patients), whereas complete blood count revealed leukocyte elevations in 8%. The authors concluded that prolonged EEG is useful if unconsciousness is prolonged, and imaging is recommended in all cases because of the relatively high yield of studies that direct acute management. Thus, this study provides valuable insights into the yield of the most commonly performed studies in children who have SE as their first seizure. A limitation may be the restriction of the study population to only those with continuous convulsive seizures, given the potential significance of shorter duration seizures (8).

From this and other studies, a variety of variables emerges that is likely important for the optimal evaluation and management of children with SE. The list includes but is not limited to the following: type of status (e.g., convulsive, nonconvulsive), duration, suspected etiology, first presentation of seizures/well-controlled known epilepsy/refractory epilepsy, baseline neurologic status, known medical/neurologic/developmental history, and family history of seizures. These factors were considered in a thoughtful review of SE in children that suggests different evaluation approaches based upon the clinical context (9). One can imagine a large-scale, multi-center study in which this information is collected in a prospective fashion at the time of presentation, followed by a stringent evaluation protocol. Data analysis could then determine which tests are of the highest yield (and lowest cost) for children who may cluster into one or more groups based on variables obtainable at the time of presentation.

by Jeffrey Buchhalter, MD, PhD, FAAN

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## *Epilepsy Currents Journal*

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