GUIDELINE FOR THE EVALUATION AND MANAGEMENT OF STATUS EPILEPTICUS (SE) 2012

(THE NEUROCRITICAL CARE SOCIETY)

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INTRODUCTION

- **SE**: requires emergent, targeted treatment to reduce patient morbidity and mortality.
- These guidelines were developed to address evaluation and management of SE in critically ill adults and children and will not address the management of SE in neonates.

DEFINITION

SE was defined as 5 min or more of

- continuous clinical and / or electrographic seizure activity

OR

- recurrent seizure activity without recovery (returning to baseline)between seizures

DEFINITION

This definition was adopted for the following reasons:

- Most clinical and electrographic seizures last less than 5 min and seizures that last longer often do not stop spontaneously
- Animal data suggest that permanent neuronal injury and pharmacoresistance may occur before the traditional definition of 30 min of continuous seizure activity have passed
- More recently, experts have suggested a revised definition of SE which includes seizures lasting for 5 min or longer although some controversy still remains

CLASSIFY

- **Convulsive SE**: defined as convulsions that are associated with rhythmic jerking of the extremities
- **Non-convulsive SE**: defined as seizure activity seen on electroencephalogram (EEG) without clinical findings associated with generalised convulsive SE
- **Refractory SE**: patients who continue to experience either clinical or electrographic seizures after receiving adequate doses of an initial benzodiazepine followed by a second acceptable antiepileptic drug (AED) will be considered refractory

METHODOLOGY

- A PubMed/Medline literature search was performed for relevant articles published through August 2011
- Clinical trials, meta-analyses, review articles, and practice guidelines were all eligible for inclusion

EVIDENCE RATING SYSTEM

Class category	Level of evidence
I Intervention is useful and effective. **II a** Evidence/expert opinion suggest intervention is useful./effective. **II b** strength of evidence/ expert opinion about intervention usefulness/effectiveness is less well establish. More data are needed; however, using this treatment when warranted is unreasonable **III** Intervention is not useful or effective or may be harmful.	**A** Adequate evidence is available from multiple, large RCTs or meta-analyses **B** Limited evidence is available from less rigorous data , including fewer, smaller RCTs, nonrandomized and observational analyses. **C** Evidence relies on expert/ consensus opinion, case reports,or standard of care

Critical care treatment

Critical care treatment	Timing
Non-invasive airway protection and gas exchange with head positioning	0–2 min
Intubation (if airway/gas exchange compromised or elevated ICP suspected)	0–10 min
Vital signs: O2 saturation, BP, HR	0–2 min
Vasopressor support of BP if SBP <90 mmHg or MAP <70mmHg	5–15 min
Finger stick blood glucose	0–2 min
Peripheral IV access	0–5 min
1. Emergent initial AED therapy (i.e.benzodiazepine)	
2. Fluid resuscitation	
3. Nutrient resuscitation (thiamine given before dextrose; dextrose)	

Critical care treatment

Critical care treatment	Timing
Urgent SE control therapy with AED	5–10 min
Neurologic exam	5–10 min
Triage lab test panel	5 min
Refractory SE treatment	20–60 min after 2nd AED
Urinary catheter	0–60 min
Continuous EEG	15–60 min
Diagnostic testing (selection depends on clinical presentation):CT, LP, MRI	0–60 min
Intracranial pressure monitoring (depending on clinical presentation)	0–60 min

Treatment recommendations for SE

Emergent treatment	Class/Level of evidence
Lorazepam	Class I, level A
Midazolam	Class I, level A
Diazepam	Class IIa, level A
Phenytoin/fosphenytoin	Class IIb, level A
Phenobarbital	Class IIb, level A
Valproate sodium	Class IIb, level A
Levetiracetam	Class IIb, level C

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Treatment recommendations for SE

Urgent treatment	Class/Level of evidence
Valproate sodium	Class IIa, level A
Phenytoin/fosphenytoin	Class IIa, level B
Midazolam (continuous infusion)	Class IIb, level B
Phenobarbital	Class IIb, level C
Levetiracetam	Class IIb, level C

Treatment recommendations for SE

Refractory treatment	Class/Level of evidence
Midazolam	Class IIa, level B
Propofol	Class IIb, level B
Pentobarbital/thiopental	Class IIb, level B
Valproate sodium	Class IIa, level B
Levetiracetam	Class IIb, level C
Phenytoin/fosphenytoin	Class IIb, level C
Lacosamide	Class IIb, level C
Topiramate	Class IIb, level C
Phenobarbital	Class IIb, level C

Summary

1. The treatment of convulsive SE should occur rapidly and continue sequentially until clinical seizures are halted (strong recommendation, high quality).
2. The treatment of SE should occur rapidly and continue sequentially until electrographic seizures are halted (strong recommendation, moderate quality).
3. Critical care treatment and monitoring should be started simultaneously with emergent initial therapy and continued until further therapy is consider successful or futile (strong recommendation, moderate quality).

Summary

4. Treatment options
   a. Benzodiazepines should be given as emergent initial therapy (strong recommendation, high quality).
      i. Lorazepam is the drug of choice for IV administration (strong recommendation, moderate quality).
      ii. Midazolam is the drug of choice for IM administration (strong recommendation, moderate quality).
      iii. Rectal diazepam can be given when there is no IV access and IM administration of midazolam is contraindicated (strong recommendation, moderate quality).

Summary

4. Treatment options
   b. Urgent control AED therapy recommendations include use of IV fosphenytoin/phenytoin, valproate sodium, or levetiracetam (strong recommendation, moderate quality).
   c. Refractory SE therapy recommendations should consist of continuous infusion AEDs, but vary by the patient's underlying condition (strong recommendation, low quality).
   d. Dosing of continuous infusion AEDs for RSE should be titrated to cessation of electrographic seizures or burst suppression (strong recommendation, very low quality).
   e. A period of 24–48 h of electrographic control is recommended prior to slow withdrawal of continuous infusion AEDs for RSE (weak recommendation, very low quality).

Summary

4. Treatment options
   f. During the transition from continuous infusion AEDs in RSE, it is suggested to use maintenance AEDs and monitor for recurrent seizures by cEEG during the titration period. If the patient is being treated for RSE at a facility without cEEG capabilities, consider transfer to a facility that can offer cEEG monitoring (strong recommendation, very low quality).
   g. Alternative therapies can be considered if cessation of seizures cannot be achieved; however, it is recommended to reserve these therapies for patients who do not respond to RSE AED treatment and consider transfer of the patient if they are not being managed by an ICU team that specialize in the treatment of SE and/or cannot provide cEEG monitoring (weak recommendation, very low quality).

PEDIATRIC SE

- There is no evidence that children respond differently to AED treatment than adults
- Young children with epilepsy who develop SE should receive IV pyridoxine in case they have pyridoxine dependent seizures
- Concern exists for possible hepatotoxicity when using valproate sodium in younger children (<2 years of age), especially those with a metabolic or mitochondrial disorder.
- There have been several pediatric series that have used diazepam as a continuous infusion with doses ranging from 0.01 to 0.03 mcg/kg/min to control RSE, but this is not a widely used current practice

Thanks for your attention!