

# Status Epilepticus (SE)

Updated: April 25, 2010

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## STATUS EPILEPTICUS (SE):

- continuous** seizure activity (clinical or electrical)  $\geq 30$  min.
- repetitive** seizures with incomplete neurological recovery interictally for period  $\geq 30$  min.

Acute life-threatening emergency that demands prompt diagnosis and treatment if severe neurological sequelae (pathologic brain changes) and death are to be minimized!

N.B. **SE duration is major determinant of morbidity and mortality!**

## ETIOLOGY

- Acute CNS insults** (50%) - anoxia, head injury, stroke, neoplasm, infection, ethanol withdrawal or intoxication (!!!).
    - **fever & infection** are most common (35%) precipitants in **CHILDREN**; *prolonged febrile seizure* is most common cause in children  $< 3$  yr.
    - **cerebrovascular disease** predominates (25%) in **OLDER ADULTS**.
  - Therapy related** (20%) - medication adjustments, **noncompliance** (most common cause in pre-known epileptic patients! esp. with abrupt phenobarbital withdrawal)
  - Undetermined cause** (30%); may be as first manifestation of idiopathic epilepsy.
- **children** comprise up to 70% of all SE cases; most other patients are **elderly!**
  - $> 50\%$  SE patients do not have history of epilepsy!
  - 5-15% epileptic patients have had one or more SE episodes at some time.

## PATHOLOGY

- in animals, neurons begin to die *after 20-60 minutes of continuous discharging* (precise time period in humans is unknown).
- significant increases in cerebral blood flow and metabolic rate during SE.
- neuron death may result from:
  - 1) metabolic **exhaustion**
  - 2) damage by **excitatory neurotransmitters**
- most vulnerable areas - hippocampus, amygdala, cerebellum, middle cortical areas, thalamus.
- acute MACROSCOPIC changes - venous congestion, small petechial hemorrhages, edema.
- MICROSCOPIC changes: ischemic cellular changes  $\rightarrow$  microglial proliferation, neuronophagia  $\rightarrow$  cell loss  $\rightarrow$  increased numbers of reactive astrocytes.

## CLASSIFICATION & CLINICAL FEATURES

- generalized** or **partial**
- convulsive** or **nonconvulsive**.

**Generalized convulsive SE (GCSE)** - convulsive activity accompanied by coma and epileptiform activity on EEG (EEG is not required for diagnosis):

*Most frequent (75%) and most dangerous type of SE!*

- 1) **tonic-clonic**
- 2) **tonic**
- 3) **clonic**
- 4) **myoclonic**

**Nonconvulsive SE** (clouding\* of consciousness  $\pm$  minor motor manifestations; i.e. abrupt-onset sustained confusional-delirious state):

\*not complete loss (so sometimes called "twilight" form of SE)

- 1) **absence SE** (75% patients  $< 20$  yrs; most other – older adults) - usually presents as one continuous episode.
- 2) **complex partial SE** - usually recurring cycles of 2 distinctly separate phases (ictal and interictal).

N.B. patients can appear totally functional - clinical picture may be so subtle that only recognizable to friends and family!

- if patient is comatose, it most likely represents “burned-out” GCSE (i.e. subtle SE).
- **EEG is required for diagnosis** (and to distinguish two types):
  - absence SE** – continuous 1-2.5 Hz generalized spike-wave activity ("spike-wave stupor");
  - complex partial SE** - ictal activity is localized (usually to frontal or temporal lobes).

**Simple partial SE** – rare; diagnosis clinical (EEG frequently negative).

- **clonic simple partial SE** is called **EPILEPSIA PARTIALIS CONTINUA**. see p. E9 >>

**GCSE manifestations change over time** - paradoxical evolution of apparent clinical improvement (inexperienced clinician may stop treatment because of apparent improvement):

- SE begins with series of generalized tonic, clonic, or tonic-clonic seizures (**OVERT SE**);
  - each seizure is discreet; motor activity stops abruptly, coincident with end of electrographic seizure.
  - each convulsion is followed by gradual recovery, and then next seizure occurs.
- if SE is not treated, discrete convulsions give way to increasingly subtle clinical manifestations (**SUBTLE SE**); e.g. only nystagmoid jerks of eyes or shoulder twitching may be seen.
  - occasionally, subtle SE occurs without prior convulsive activity (e.g. in severe diffuse cerebral dysfunction).
- eventually, coma without motor activity is all that remains, although electrographic seizures persist (**ELECTRICAL SE**).
  - N.B. status epilepticus should be suspected in any unexplained coma (e.g. patient stops having overt seizures, yet remains comatose)

Treatment should be continued until **electrographic seizure activity\*** has resolved completely!

\*CNS injury can occur even when patient is paralyzed with neuromuscular blockade but continues to have electrographic seizures.

GCSE produces **SYSTEMIC EFFECTS**:

**Permanent brain damage** is caused more by **ongoing seizure activity** than by **systemic factors!**

- 1) **hypoxia**, respiratory and metabolic **acidosis**
  - convulsive SE affects mechanical aspects of breathing (respiratory fatigue) + can cause neurogenic pulmonary edema + aspiration.
  - medications used for treating SE (esp. benzodiazepines and barbiturates) inhibit respiratory drive.
- 2) cerebral dysautoregulation, **BP instability** (↑ then ↓)
- 3) **hyperpyrexia** up to 42°C (motor activity + central sympathetic drive)
- 4) acute hypercatecholaminemia may trigger fatal cardiac arrhythmias.
- 5) hyperazotemia; hypokalemia; hyponatremia; hyperglycemia → hypoglycemia.
- 6) **rhabdomyolysis** → myoglobinuria, acute tubular necrosis, renal failure.
- 7) ↑↑↑ of plasma prolactin, glucagon, growth hormone, ACTH.
- 8) **leukocytosis** (bands should not be seen in absence of infection); modest **CSF pleocytosis**.

## DIFFERENTIAL DIAGNOSIS

SE diagnosis depends on demonstrating ictal patterns in EEG!

Neuroimaging has no impact on immediate management until seizures are controlled.

1. **Nonepileptic phenomena** (tremor, myoclonus, eye and oral-buccal movements that follow anoxia, brain stem or bilateral cerebral ischemia, drug overdose, severe metabolic disturbances) - difficult to differentiate clinically from nonconvulsive SE.
2. Prolonged **psychogenic seizures**.

## MANAGEMENT

- **seizure activity ≥ 5-10 minutes** - treat as status, because most seizures must terminate spontaneously within 1-2 minutes.

If seizure lasts > **2 minutes**, place *intravenous line* and *draw blood* for tests  
If seizure continues **beyond 5 minutes**, begin treatment with *benzodiazepine*

- **impending status epilepticus** - 3 or more TCS within 24-hour period (esp. if this represents increase from typical frequency); H: home treatment with rectal **DIAZEPAM** gel (Diastat) 10-20 mg (0,05-0,1 mg/kg) should be considered before transfer to ED.  
N.B. infusing **MIDAZOLAM** into mouth (between gums and cheek) is twice as effective as rectal DIAZEPAM!
- admit to ICU, set a clock in motion.

N.B. *use of neuromuscular blockers is inappropriate* because they do not stop seizure activity in brain (which is cause of brain damage!).

### Treatment for GCSE

#### STEP 1 – ABC + Coma see p. S30 >>

1. Secure oral airway (e.g. tongue may cause obstruction in younger patient - place nasopharyngeal airway), prevent aspiration (turn head to side, suction secretions), administer 100% O<sub>2</sub> (via properly fitting face mask)
2. **Monitor** - ECG, SaO<sub>2</sub>, vital signs.
3. **Blood tests** - bedside glucose test; draw blood for AEDs levels (if indicated), CBC, chemistries (electrolytes, Ca<sup>2+</sup>, Mg<sup>2+</sup>, BUN, creatinine), toxicological screens.
4. **Establish intravenous line** with normal saline.
5. **THIAMINE** 100 mg IV → **DEXTROSE** 50% 50 ml IV (D25 2 ml/kg in children).
6. Search for probable cause of SE (tests should not impede rapid and aggressive treatment!):
  - 1) obtain **history**
  - 2) perform **examination**
  - 3) some authors feel that **EEG monitoring** should be routine part of treatment; others use EEG only selectively (e.g. when GCSE diagnosis in doubt, assessing treatment adequacy).  
In general, EEG has no role in management of GCSE!
  - 4) **neuroimaging** should be done in all patients (except children with febrile SE); CT is sufficient to exclude acute brain lesion; MRI should be obtained later if CT was normal.
  - 5) **lumbar puncture** is performed in any febrile patient (even if signs of meningitis are not present); if ICP↑ or mass lesion are suspected, antibiotics should be given immediately and CT scan obtained first.

#### STEP 2 – intravenously administer **ANTICONVULSANTS** (terminate 80-90% cases):

- continuously monitor for respiratory depression, hypotension, cardiac arrhythmias.
  - advanced cardiac life support must be ready!
1. **Rapid-acting** anticonvulsant **DIAZEPAM** 0.2 mg/kg (0.1-1.0 mg/kg in children) at 1-5 mg/min up to 10 mg; repeat once or twice q5-30min if seizures persist.
    - diazepam (high lipid solubility and rapid CNS entry) frequently abolishes seizure activity within minutes, only for seizures to recur within 30 minutes (as drug redistributes to other fatty tissues).
    - preferred (over diazepam)\* alternative - **LORAZEPAM** 0.1 mg/kg (0.05-0.5 mg/kg in children) at 2 mg/min up to 4 mg.  
\*less respiratory depression, less fat soluble - slower, but **longer duration of action** – up to 2-3 hours!!!  
N.B. even though lorazepam has much shorter T<sub>1/2</sub> than diazepam, its effective half-life in brain is longer.
    - if IV access is not obtainable, diazepam is drug of choice - may be given rectally (0.5 mg/kg, maximum 20 mg), endotracheally, intraosseously.
  2. Immediately next step (to prevent seizure recurrence) – **long-acting** anticonvulsant **PHENYTOIN** 15-20 mg/kg load (up to 50 mg/min or 1 mg/kg/min); if seizures persist → additional 5-10 mg/kg boluses q20min (up to 30 mg/kg total or 30 µg/ml level).  
N.B. phenytoin is incompatible with glucose-containing solutions!
    - use **continuous ECG and BP monitoring** during infusion! (phenytoin is contraindicated in heart block).
    - better alternative - **FOSPHENYTOIN** 15-20 mg PE/kg (up to 150 mg PE/min); PE = phenytoin equivalents.
    - alternative (in hypersensitive to PHT or patients who already are taking PHT but in whom blood level of PHT is not yet known\*) - IV **VALPROATE** (slow onset of action is drawback).  
\* administering fosphenytoin to patient who is taking PHT may raise level to point at which PHT actually becomes proconvulsant!

N.B. most common cause of treatment failure - appropriate medication administered in **inadequate dosages** via **inappropriate route**!

- **acidosis** should not be treated (acidosis does not correlate with degree of neuronal injury + acidosis is anticonvulsant).
- **hyperthermia** should be treated aggressively (correlates with poor neurological outcome) - fans and antipyretics.

#### STEP 3 (terminates 94% cases):

1. Elective **intubation** (because benzodiazepine + barbiturate will cause respiratory depression) using rapid sequence technique (because all patients are considered as having full stomach).
2. Place **arterial line** + draw **arterial blood gases**.
3. **PHENOBARBITAL** IV 20 mg/kg q20min (100 mg/min or 3 mg/kg/min in children) up to total 1-2 g.  
N.B. monitor for respiratory depression! - assisted ventilation is usually required!

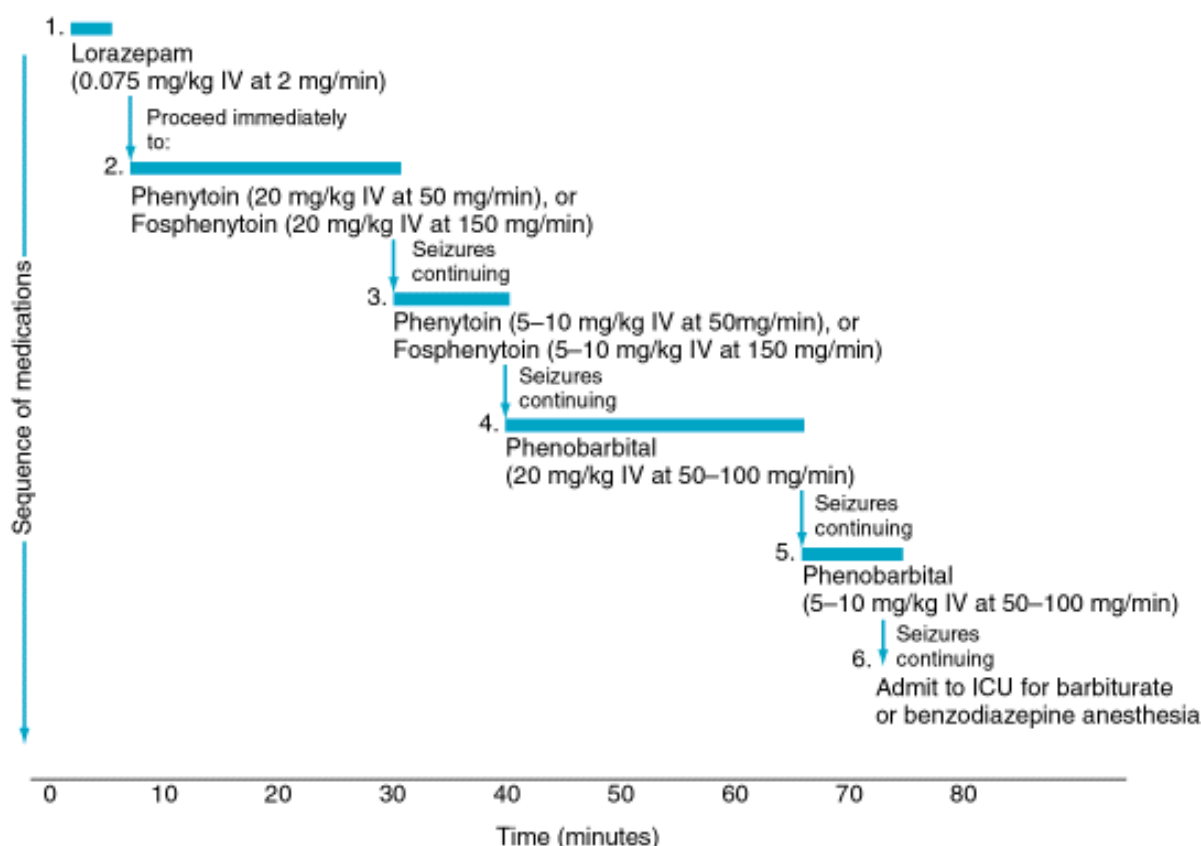
- SE that is not controlled with standard dosages of benzodiazepines, phenytoin, phenobarbital is considered **REFRACTORY SE**.

**STEP 4 – pharmacological COMA** (administered by anesthesiologist):

**PENTOBARBITAL** 3-15 mg/kg load → 0.5-5 mg/kg/hr maintenance (titrated to *burst-suppression* near-electrocortical silence).

- treatment is continued for 6-48 hours.
- continuously monitor EEG (for recurrence of seizure activity).
- high risk of hypotension - ventilatory assistance and vasopressors are invariably required.
- other drugs used for refractory SE; however, experience is limited:
  - PROPOFOL** (1-2 mg/kg → 2-10 mg/kg/h)
  - MIDAZOLAM** (0.2 mg/kg → 0.75-45 µg/kg/min)
  - DIAZEPAM** drip ≈ 2-3 mg/hr.
  - PARALDEHYDE** 5% (150-200 mg/kg IV slowly for 15-20 min → 20 mg/kg/hr in concentration in glass\* bottle); if administered rectally or IM can produce tissue damage and sloughing! \*drug is incompatible with plastic
  - LIDOCAINE** (may cause seizures in toxic doses)

**STEP 5 – general anesthesia** using inhaled anesthetic (**HALOTHANE** < **ISOFLURANE**).



**Treatment for NONCONVULSIVE STATUS** - *may be treated less aggressively* - risk of neurological sequelae is significantly lower!

- good guideline is not to worsen patient's level of consciousness by pharmacologic means.

**ABSENCE SE**: low doses of **benzodiazepine** → dramatic improvement in mental state → **VALPROATE** IV or rectally (20-25 mg/kg in 50-mL solution over 10 minutes; repeat after 3 hours, then q6h) or oral **ETHOSUXIMIDE**.

- no deaths or long-term morbidity have been reported!
- differentiation from other causes is important - many mimics of absence SE can lead to irreversible neuronal damage if not aggressively treated!

**COMPLEX PARTIAL SE** – treatment as for GCSE:

- intravenous **benzodiazepines**.
  - FOSPHENYTOIN** (IM or IV)
  - oral** anticonvulsants
- negative outcomes can occur!

**SIMPLE PARTIAL SE** – treatment less aggressive as for GCSE (e.g. if first-line drugs are ineffective, clinician may elect not to use general anesthetic agent to stop simple partial SE).

**MANAGEMENT FOLLOWING STATUS EPILEPTICUS**

- idiopathic status epilepticus in previously healthy patient* → maintain **AED therapy for 3 months** → discontinue if remains asymptomatic.
- other cases* – as general principles require. see p. E5 >>

**PROGNOSIS**

Morbidity & mortality depend on:

- intervention speed** (duration > 1 hour carries poor prognosis)
- age** (outcome is better in children)
- etiology** (outcome is better with pre-existing idiopathic epilepsy, drug-induced SE).

**Mortality (within 30 days) ranges 1-65%** (death caused directly by SE per se occurs in 2-10% cases)
 

- 27% for overt GCSE; 65% for *subtle GCSE*
- 4% in children, 13% in young adults, 38% in elderly, > 50% in *those > 80 years*.

**BIBLIOGRAPHY** for ch. “Epilepsy and Seizures” → follow this [LINK](#) >>