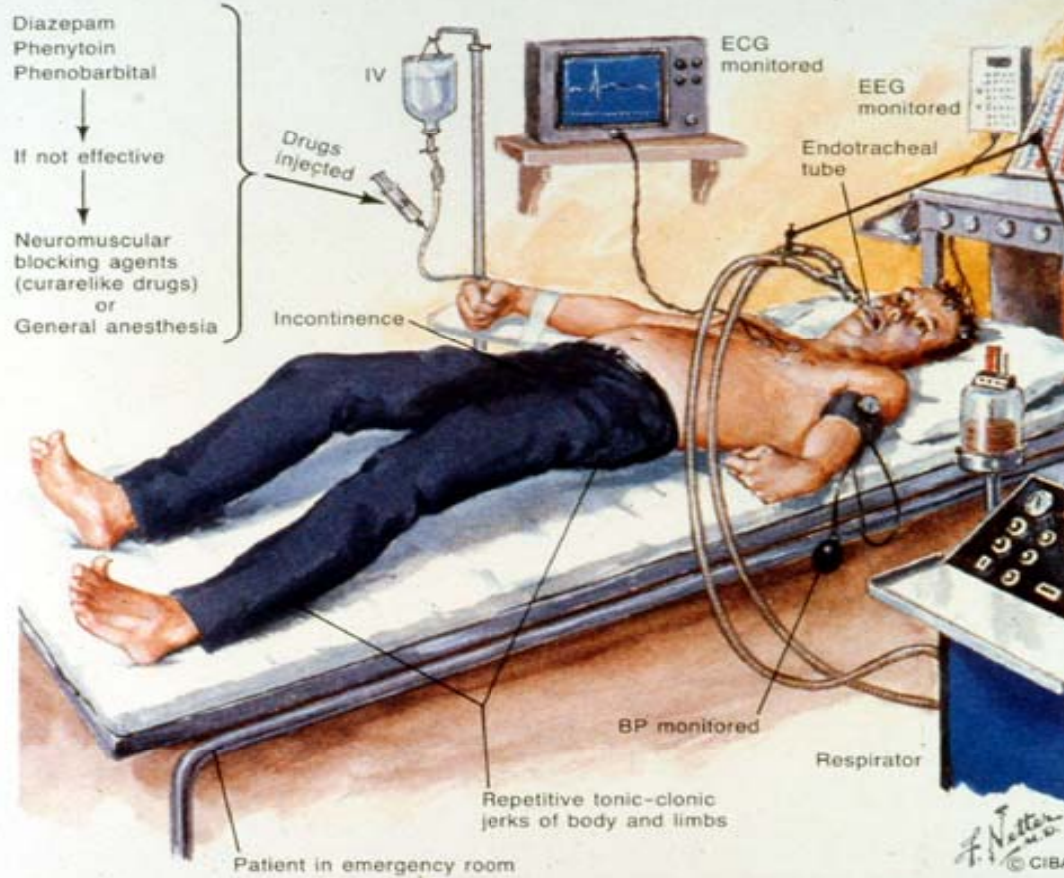


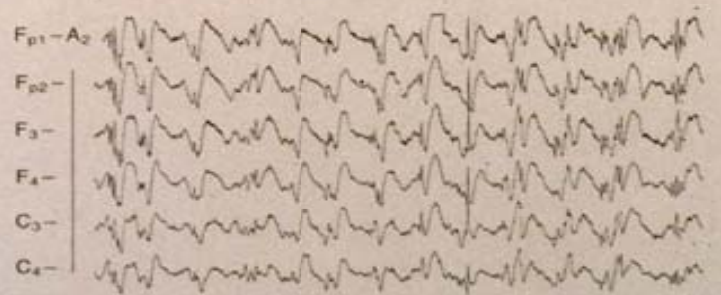
Status Epilepticus: Clinical Features, Pathophysiology, and Treatment

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Status Epilepticus



EEG: status epilepticus



Continuous repetitive generalized spike-and-wave discharges

Status Epilepticus: Definitions

Basic

State of continuing or recurring seizures in which recovery is incomplete

Official

Condition characterized by an epileptic seizure that is so frequently repeated or so prolonged as to create a fixed and lasting condition

Pathophysiologic

Any seizure activity lasting longer than 30 minutes

Classification of Status Epilepticus

- **Generalized Convulsive Status Epilepticus**
 - **Tonic-clonic status epilepticus**
 - **Tonic status epilepticus**
 - **Clonic status epilepticus**
 - **Myoclonic status epilepticus**
- **Generalized Nonconvulsive Status Epilepticus**
 - **Absence status epilepticus**

Classification of Status Epilepticus (continued)

- **Simple Partial (Focal) Status Epilepticus**
 - **Somatomotor status epilepticus**
 - **Epilepsia partialis continua**
 - **Sensory status epilepticus**
 - **Somatosensory**
 - **Special sensory**
 - **Aphasic status epilepticus**
 - **Autonomic status epilepticus**
- **Complex Partial Status Epilepticus**

Status Epilepticus: Epidemiology

Incidence

~ 60,000 cases of generalized tonic-clonic status per year in U.S.

- 1/3 consist of first seizure of a recurrent problem (i.e., epilepsy)
- 1/3 in patients with prior diagnosis of epilepsy
- 1/3 in patients without a history of epilepsy

Most frequent in children and patients >60 years old

Mortality

1-2% from seizures

10% from underlying illness

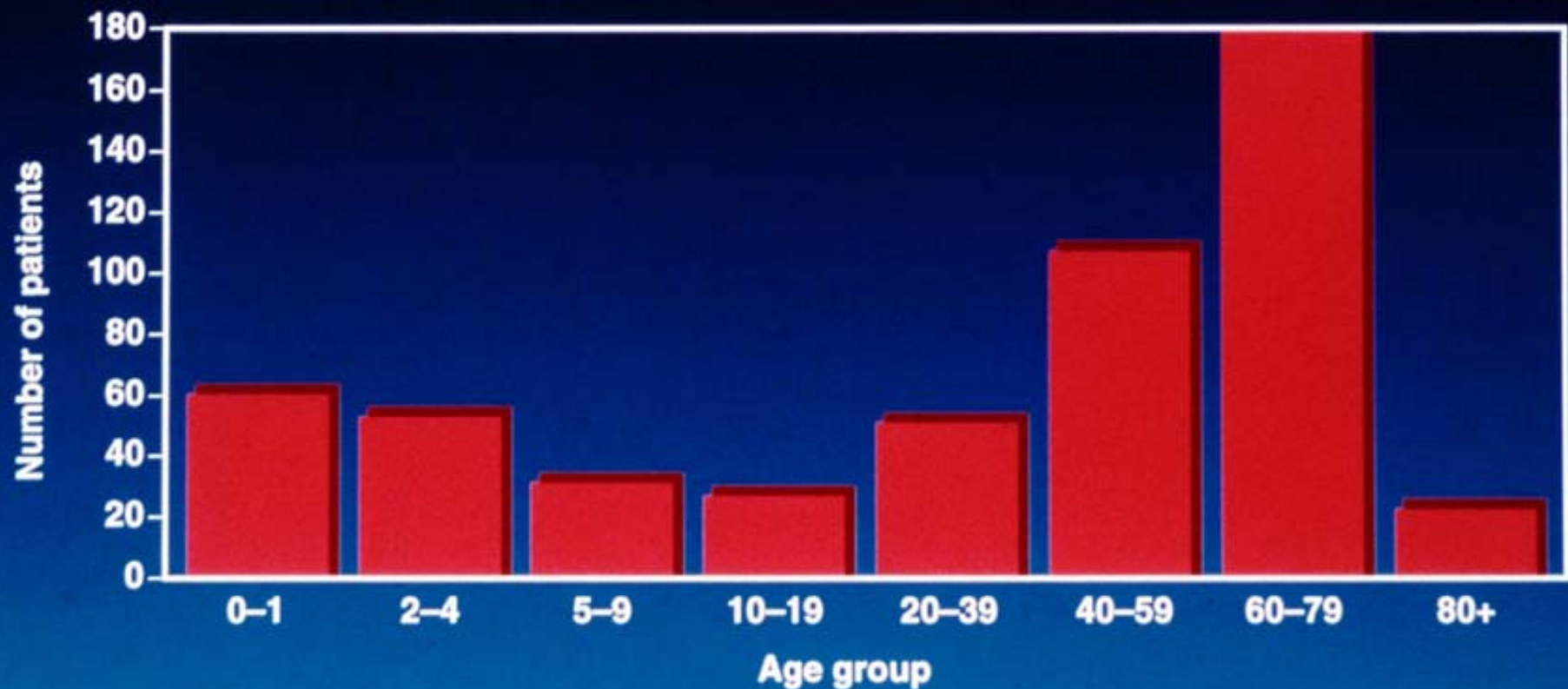
Annual hospital visits for acute seizure

Annual hospital visits for acute seizure

- **368,000 patient visits to emergency rooms***
 - 50,000 breakthrough seizures are treated annually
- **Status epilepticus (SE)**
 - 50,000 to 60,000 annually
 - 1% to 8% of all hospital admissions
 - First seizure in 12% of patients

Age distribution of status epilepticus

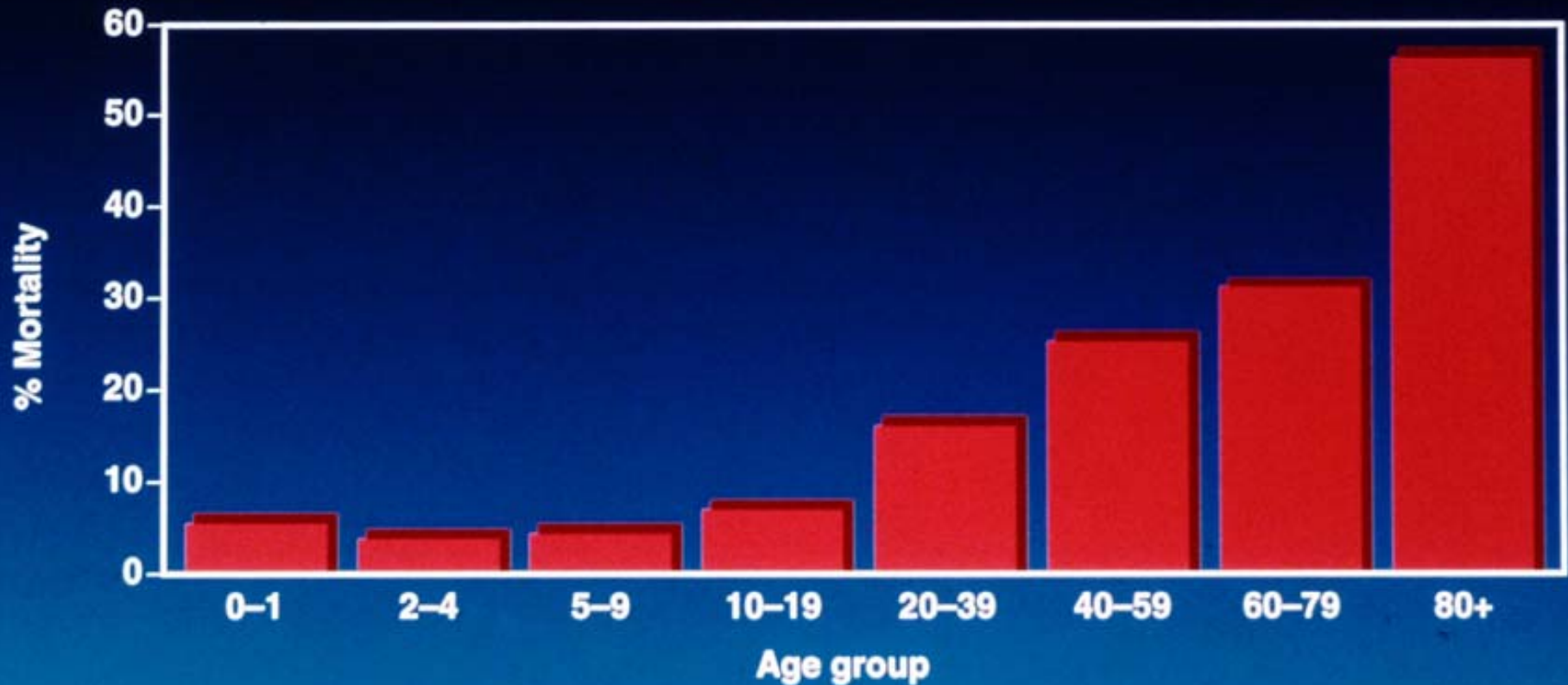
Age distribution of status epilepticus cases in Richmond, Virginia from 1982 to 1989. 1982 to 1989 retrospective data base (n=546).



DeLorenzo RJ, et al. Status epilepticus in children, adults, and the elderly. *Epilepsia*. 1992;33(suppl 4):515-525.

Mortality in status epilepticus by age group

Percent mortality by age group among 546 patients with status epilepticus in Richmond, Virginia from 1982 to 1989.



DeLorenzo RJ, et al. Status epilepticus in children, adults, and the elderly. *Epilepsia*. 1992;33(suppl 4):515-525.

Status Epilepticus: Etiology

Head trauma

Drug/alcohol abuse or withdrawal

CNS tumor

Congenital CNS abnormality

CVA

Fever, acute systemic or metabolic illness

CNS infection

AED noncompliance

Idiopathic – 15-30%

Status Epilepticus: Morbidity and Mortality

- **CNS damage due to underlying illness or acute insult**
- **CNS damage due to repeated seizures**
- **Systemic and metabolic factors related to repeated GTCS**

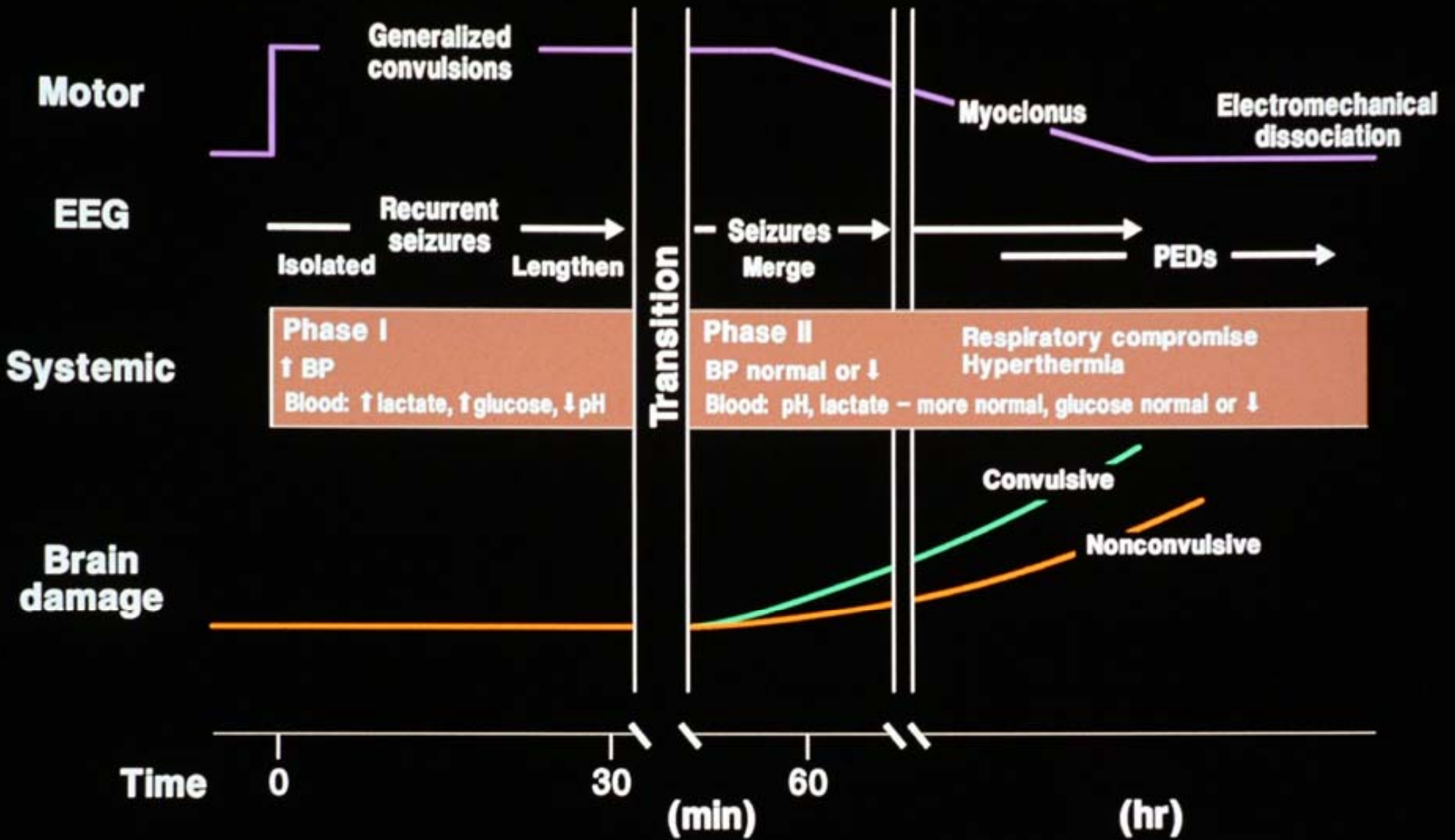
Status Epilepticus: Pathophysiology

- **Status epilepticus has a distinct natural history**
- **More prolonged the status, the more intractable to treatment it is**
- **More prolonged the status, the poorer the prognosis**

EEG Patterns in Status Epilepticus

- 1. Discrete seizures with interictal slowing**
- 2. Waxing and waning of ictal discharges**
- 3. Continuous ictal discharges**
- 4. Continuous ictal discharges punctuated by flat periods**
- 5. Periodic epileptiform discharges on a flat background**

Status Epilepticus: Systemic and Brain Metabolism I

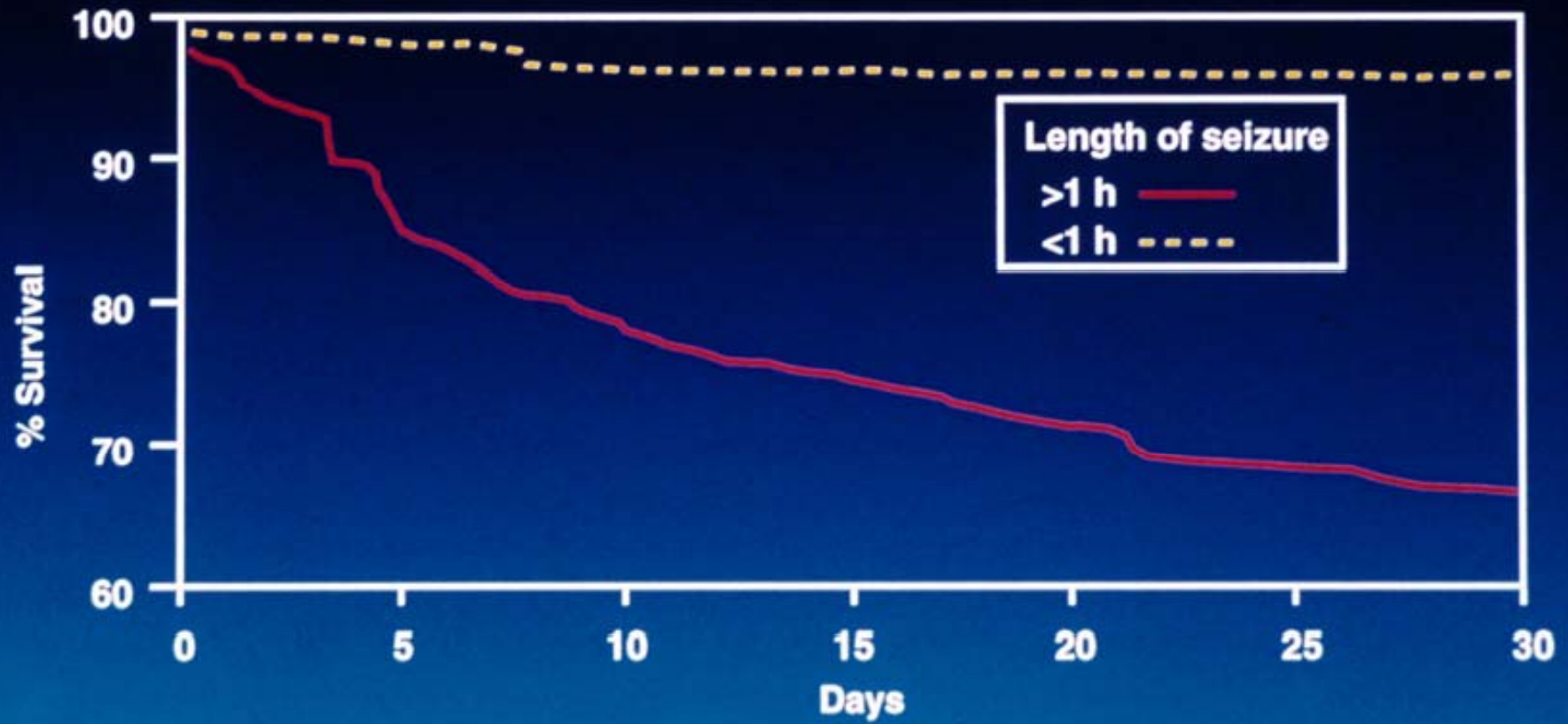


Status Epilepticus: CNS Consequences

- Prolonged status** **Damage to cerebral cortex, cerebellum, thalamus, amygdaloid body, hippocampus**
- Childhood status** **May lead to hippocampal sclerosis and complex partial seizures later in life**
- Mechanisms** **Reduced GABA inhibition**
Enhanced glutaminergic excitation
Calcium mediated cell damage

Survival in status epilepticus by duration of seizure

Survival curves for prolonged (solid line) and nonprolonged (dashed line) seizure duration. The data are presented as percent survival based on a 30-day follow-up period.



Major drugs used to treat status epilepticus

The major drugs used to treat status epilepticus: intravenous (IV) doses, pharmacokinetics, and major toxicities*

	Diazepam	Lorazepam	Phenytoin	Phenobarbital
Adult IV dose (mg/kg), range (total dose)	0.15–0.25	0.1 (4–8 mg)	15–20	20
Maximal administration rate (mg/min)	5	2.0	50	100
Time to stop status (min)	1–3	6–10	10–30	20–30
Effective duration of action (h)	0.25–0.5	>12–24	24	>48

*Data modified from Treiman.

Working Group on Status Epilepticus. Treatment of convulsive status epilepticus. *JAMA*. 1993;270:854-859.

Treatment of Status Epilepticus

Time Frame

Procedure

0-5 min

Obtain vital signs, establish airway, administer oxygen if needed.

Observe seizures briefly to ascertain that patient is really in status.

Draw baseline blood work (CBC, chemistry panel, antiepileptic drug levels), draw ABGs (for pO₂ and pH), draw toxicology screen.

Quickly assess patient for signs of cardio-respiratory compromise, hyperpyrexia, focal neurologic signs, head trauma, CNS infection.

Treatment of Status Epilepticus

Time Frame

Procedure

6-9 min

Start IV infusion with saline solution.

Administer 100 mg thiamine, IV.

Administer 50 ml of 50% glucose solution, IV, if blood sugar is low or unobtainable.

Do not give glucose if blood sugar is normal or high.

Always have CPR equipment at bedside of a patient in status.

Treatment of Status Epilepticus

Time Frame

Procedure

10-45 min Infuse lorazepam (Ativan), 0.1 mg/kg, at 2 mg/min.

Begin IV loading dose of fosphenytoin (Cerebyx), 20 mg PE/kg, at 150 mg/min.

Monitor patient's B/P, pulse, EKG, and respirations while giving IV fosphenytoin and lorazepam.

Side effects: hypotension, arrhythmia, paresthesias, and respiratory depression.

Treatment of Status Epilepticus

Time Frame

Procedure

46-60 min If seizures persist, intubate and give phenobarbital, 20 mg/kg, at 100 mg/min.

Never use Valium and phenobarbital sequentially in the treatment of status, unless the patient is intubated and in an ICU. Their hypotensive and respiratory depressant actions synergize. Serious and abrupt side effects can occur with these two drugs when given together.

Treatment of Status Epilepticus

Time Frame

Procedure

1 hour

If seizures persist, the patient should be placed in a drug induced coma with pentobarbital, a benzodiazepine, or other anesthetic agent to prevent life threatening lactic acidosis, hypoxia, hyperthermia, and permanent seizure-induced neuronal damage. The patient must be in an ICU, and outcome should be monitored and treatment guided by EEG with the goal being suppression of seizure activity on EEG.

Protocol for Pentobarbital Coma

Setting	Intubation and ventilation EEG monitoring
Loading	5 mg/kg IV bolus 25 to 50 mg every 2 to 5 min to EEG burst suppression
Maintenance	5 mg/kg/hr
Pentobarbital concentrations	25 to 50 mg/ml
Duration	Days to weeks

Status Epilepticus: Future Treatment Modalities

VA cooperative study

To be completed in 1993

**Novel and specific
medications**

EAA receptor antagonists

GABA agonists

Specific calcium channel blockers

Phenytoin prodrug

IV valproic acid

VA Cooperative Generalized Convulsive Status Epilepticus Study

- 384 patients with convulsive status and 134 patients with subtle (NCSE) status were randomized to:
 - LZP (n=97, 39) with 0.1 mg/kg infused at 2 mg/min
 - DZP/PHT (n=95, 36) with 0.15/18 mg/kg infused at 5/50 mg/min
 - PHT (n=101, 26) with 18 mg/kg infused at 50 mg/min
 - PB (n=91, 33) with 15 mg/kg infused at 100 mg/min
- Convulsive status aborted by **LZP (65%)***, PB (58%), DZP/PHT (56%), vs **PHT (44%)*** as 1st AED (*p=0.002)
- NCSE aborted in 7-24% of cases with no differences in AEDs
- No differences among AEDs with: recurrence in 12 hours, adverse events, or outcome at 30 days

RCT of IV VPA vs IV PHT in GTC Status Epilepticus

- 68 patients with convulsive status were randomized to:
 - IV VPA (n=35) with 30 mg/kg infused at ~140 mg/min
 - IV PHT (n=33) with 18 mg/kg infused at 50 mg/min
- Status aborted by VPA (66%) vs PHT (42%) as 1st AED
- As 2nd AED (ie, 1st AED failed), status aborted by VPA (79%) vs PHT (25%)
- Adverse events ~ same (but small sample)
- IV VPA may have better efficacy than IV PHT in GTC status

Safety and Tolerability of Rapid IV Infusion Of Keppra in Healthy Controls: Summary

- Approved dosage = 500-1500mg diluted in ≥ 100 ml of diluent as a 15-minute IV infusion (33 – 100 mg/min) bid
- This study demonstrates that IV LEV is well tolerated in healthy subjects at dosages and infusion rates greater than those proposed
- Adverse events were mild or moderate in intensity and resolved within 8-24 hours
- No clear relation was found between the incidence of AEs and LEV dose or duration of infusion
- No clinically significant changes from baseline in lab testing, vital signs, EKG findings, or physical examinations were reported after IV LEV dosing

