Management of Status Epilepticus

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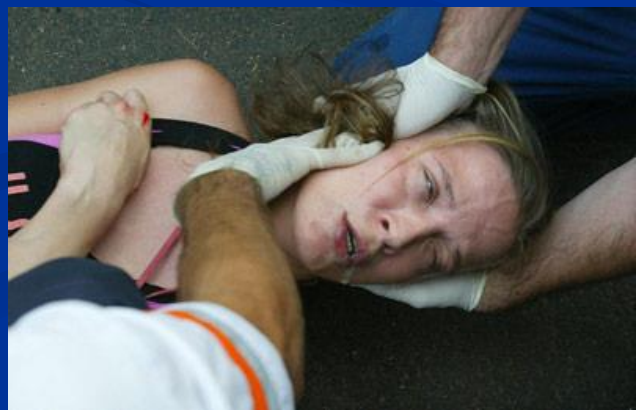


Objectives

- By the end of this lecture you should be able to know:
  - Definition of seizure and status epilepticus (SE).
  - Causes of SE
  - Approach to seizure disorders.
  - Bedside management of seizure and SE
  - Standard management protocol for SE

INTRODUCTION

- Seizures are dramatic and frightening for all who witness the event – and tend to induce panic, rather than rational thought, even on a neurology service.

- Clinical seizures are caused by an excessive, synchronous, abnormal discharge of cortical neurons that produces a sudden change in neurologic function.

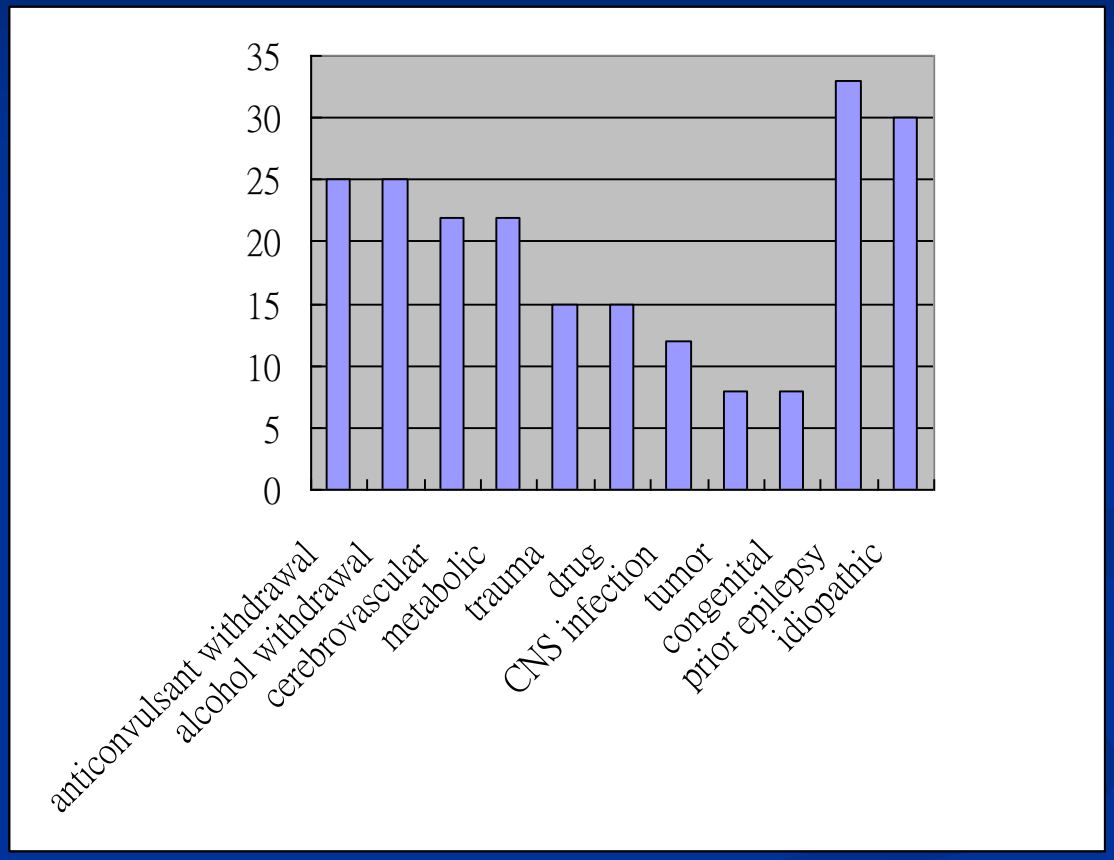
- Seizures may be *focal*, involving a single brain region and causing limited dysfunction, or they may be *generalized*, involving the whole brain and producing loss of consciousness and convulsions.

Definition of status epilepticus (SE)

	Strong Recommendations
High or Moderate Quality Evidence	•SE defined as 5 min or more of continuous clinical and/or electrographic seizure activity or recurrent seizure activity without recovery between seizures •Refractory SE should be defined as SE that does not respond to the standard treatment regimens, such as an initial benzodiazepine followed by another AED •The etiology of SE should be diagnosed and treated as soon as possible

Brophy, et al NCC 2012

Cause



The comprehensive evaluation and treatment of epilepsy,Steven C.Schachter,Donald L,Schomer

Your patient have seizure !!!!!

Patient with seizure in your ward

At night you receive a call that your patient have seizure: What you have to do ???

- **At night you receive a call that your patient have seizure: What you have to do ???**
- **Questions**

1. Is the patient still seizing? If yes, how long has it been going on?
2. What is the patient's level of consciousness?
3. Is this the first known seizure for this patient?
4. Is the patient on anticonvulsant medication?
5. Is the patient diabetic?

Orders

- **If the patient is still seizing:**
  1. Have two intravenous (IV) setups ready at the bedside.
  2. Have oral airway and Ambu bag available at the bedside.
  3. Have lorazepam 8 mg ready at the bedside. Diazepam 10 mg is an alternative.
  4. Clear any sharp or hard objects from the bed, put the side rails up, and pad the side rails.
  5. Perform a finger stick glucose test.

On the Way

- **What is the differential diagnosis of seizures?**

V (vascular): Intracranial hemorrhage, acute or chronic ischemic infarction, subarachnoid hemorrhage, arteriovenous malformation, venous sinus thrombosis.

I (infectious): meningitis or abscess .

T (traumatic): new head injury old head injury with subdural hematoma

A (autoimmune): systemic lupus erythematosus, (CNS) vasculitis.

M (metabolic/toxic): hypo- or hypernatremia, hypo- or hypercalcemia, hypomagnesemia, hyper-thyroidism, uremia, hyperammonemia, ethanol (EtOH) toxicity or EtOH withdrawal, drugs cocaine, phenycyclidine, and amphetamines

I (idiopathic/iatrogenic): idiopathic epilepsy or medications

N (neoplastic)

S (structural)

Management on Bedside

- ***Treatment of an Ongoing Seizure***

1. **Keep calm.** It is likely that others in the room are reacting with fear or panic. Ask family members to leave the room. Tell them you will speak with them as soon as the situation is evaluated and under control.
2. **Ensure that all measures have been taken to protect the patient from physical injury and aspiration of gastric contents.** Have one or two people maintain the patient in a lateral decubitus position.
3. **Administer oxygen by nasal cannula or face mask.**
4. **Watch and wait for 2 minutes.** A majority of seizures will stop spontaneously within a short time.

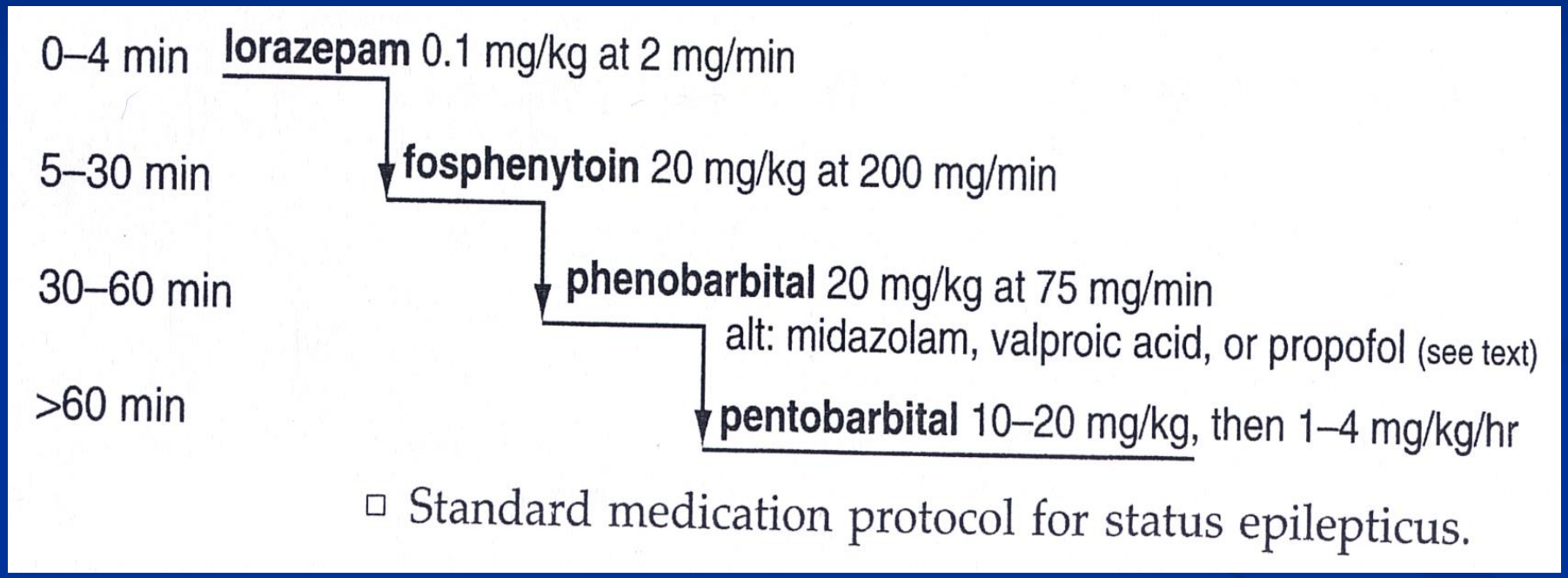
- Check the **finger stick glucose** level.
- Make sure there are **two IV setups available**, at least one with 0.9% normal saline (NS). If the patient has no IV access, start an IV line.
- Draw Diazepam 5mg IV slowly.
- **Elicit any further history** not obtained initially.
- Is this a first-ever seizure? Is the patient on anticonvulsants? What is the patient's admitting diagnosis? Is the patient diabetic? Has the patient been febrile in the last 24 hours? Ask for the chart to be brought to the bedside.
- **Observe the seizure type.**

- **If the seizure has not remitted in 2 minutes,** ensure that an IV line is available.
- Avoid the antecubital area because convulsions may cause flexion of the arm and block off the IV site.
- Order the following **blood tests:** (CBC), electrolytes, glucose, magnesium (Mg), calcium (Ca), ammonia, EtOH level, toxicology screen, and anticonvulsant level (if applicable).
- If the patient is hypoglycemic, give **glucose (50 ml of D50W).**
- If there is any history or suspicion of alcoholism, administer **thiamine 100 mg by slow, direct injection over 3 to 5 minutes.**

- **An Ambu bag with face mask should be at the bedside because benzodiazepines can cause respiratory depression.**

Treatment of Status Epileptics

- If the seizure has not stopped with a full dose of a benzodiazepine, administer **phenytoin 15 to 20 mg/kg as a slow IV infusion.** (This loading dose corresponds to approximately 1500 mg in a 70-kg patient.)
- The rate of administration should not exceed 50 mg/min because phenytoin can cause cardiac arrhythmias, prolongation of the QT interval, and hypotension.
- **(ECG)** should be monitored continuously, and the blood pressure should be checked during the infusion.
- Approximately 70% of prolonged seizures will be brought under control.
- **If the seizure lasts longer than 30 minutes, transfer the patient to an intensive care unit (ICU)** for probable intubation.

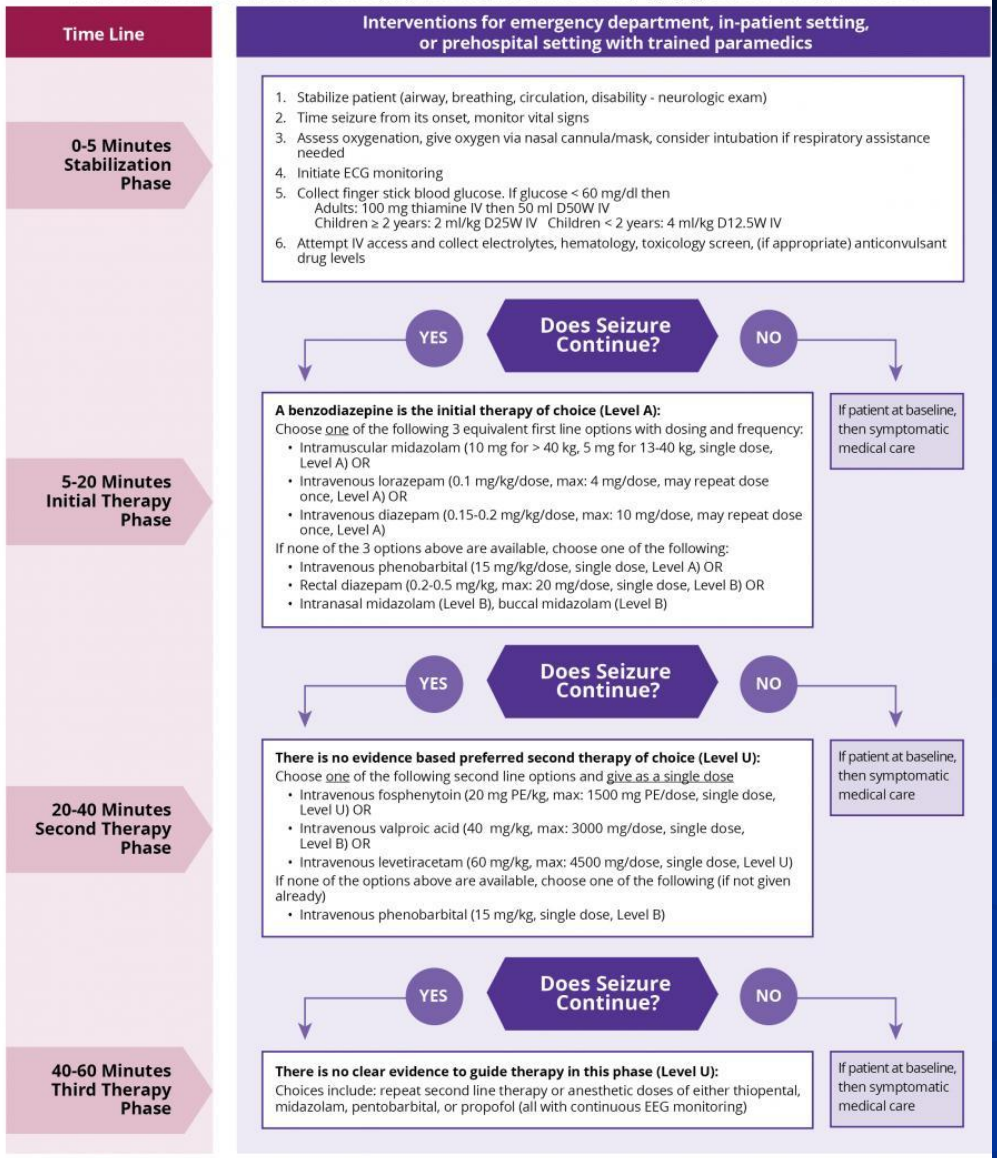


□ Standard medication protocol for status epilepticus.

- **Once the patient is in the ICU,** if the patient is continuing to seize despite a full phenytoin load, the next step is to administer barbiturates. **Phenobarbital should be infused loading dose of 15 to 20 mg/kg.**
- Twenty to 30% of patients will continue to have electrographic seizure activity that is not clinically apparent.
- Alternatives to phenobarbital include **midazolam (Versed) 0.2 mg/kg bolus, followed by IV infusion of 0.1 to 2 mg/kg/hour, propofol 3 to 5 mg/kg loading dose.**
- General anesthesia with halothane and neuromuscular blockade has been used in some cases to avoid rhabdomyolysis, but this eliminates the ability to follow the neurologic examination.

Proposed Algorithm for Convulsive Status Epilepticus

From "Treatment of Convulsive Status Epilepticus in Children and Adults," *Epilepsy Currents* 16.1 - Jan/Feb 2016



American Epilepsy Society

Disclaimer: This clinical algorithm/guideline is designed to assist clinicians by providing an analytic framework for evaluating and treating patients with status epilepticus. It is not intended to establish a community standard of care, replace a clinician's medical judgment, or establish a protocol for all patients. The clinical conditions contemplated by this algorithm/guideline will not fit or work with all patients. Approaches not covered in this algorithm/guideline may be appropriate.

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Proposed Algorithm for Convulsive Status Epilepticus

From "Treatment of Convulsive Status Epilepticus in Children and Adults," *Epilepsy Currents* 16.1 - Jan/Feb 2016

Time Line	Interventions for emergency department, in-patient setting, or prehospital setting with trained paramedics
0-5 Minutes Stabilization Phase	1. Stabilize patient (airway, breathing, circulation, disability - neurologic exam) 2. Time seizure from its onset, monitor vital signs 3. Assess oxygenation, give oxygen via nasal cannula/mask, consider intubation if respiratory assistance needed 4. Initiate ECG monitoring 5. Collect finger stick blood glucose. If glucose < 60 mg/dl then Adults: 100 mg thiamine IV then 50 ml D50W IV Children ≥ 2 years: 2 ml/kg D25W IV Children < 2 years: 4 ml/kg D12.5W IV 6. Attempt IV access and collect electrolytes, hematology, toxicology screen, (if appropriate) anticonvulsant drug levels
	YES — **Does Seizure Continue?** — NO
5-20 Minutes Initial Therapy Phase	**A benzodiazepine is the initial therapy of choice (Level A):** Choose one of the following 3 equivalent first line options with dosing and frequency: • Intramuscular midazolam (10 mg for > 40 kg, 5 mg for 13-40 kg, single dose, Level A) OR • Intravenous lorazepam (0.1 mg/kg/dose, max: 4 mg/dose, may repeat dose once, Level A) OR • Intravenous diazepam (0.15-0.2 mg/kg/dose, max: 10 mg/dose, may repeat dose once, Level A) If none of the 3 options above are available, choose one of the following: • Intravenous phenobarbital (15 mg/kg/dose, single dose, Level A) OR • Rectal diazepam (0.2-0.5 mg/kg, max: 20 mg/dose, single dose, Level B) OR • Intranasal midazolam (Level B), buccal midazolam (Level B) If patient at baseline, then symptomatic medical care
	YES — **Does Seizure Continue?** — NO
20-40 Minutes Second Therapy Phase	**There is no evidence based preferred second therapy of choice (Level U):** Choose one of the following second line options and give as a single dose • Intravenous fosphenytoin (20 mg PE/kg, max: 1500 mg PE/dose, single dose, Level U) OR • Intravenous valproic acid (40 mg/kg, max: 3000 mg/dose, single dose, Level B) OR • Intravenous levetiracetam (60 mg/kg, max: 4500 mg/dose, single dose, Level U) If none of the options above are available, choose one of the following (if not given already) • Intravenous phenobarbital (15 mg/kg, single dose, Level B) If patient at baseline, then symptomatic medical care
	YES — **Does Seizure Continue?** — NO
40-60 Minutes Third Therapy Phase	**There is no clear evidence to guide therapy in this phase (Level U):** Choices include: repeat second line therapy or anesthetic doses of either thiopental, midazolam, pentobarbital, or propofol (all with continuous EEG monitoring) If patient at baseline, then symptomatic medical care

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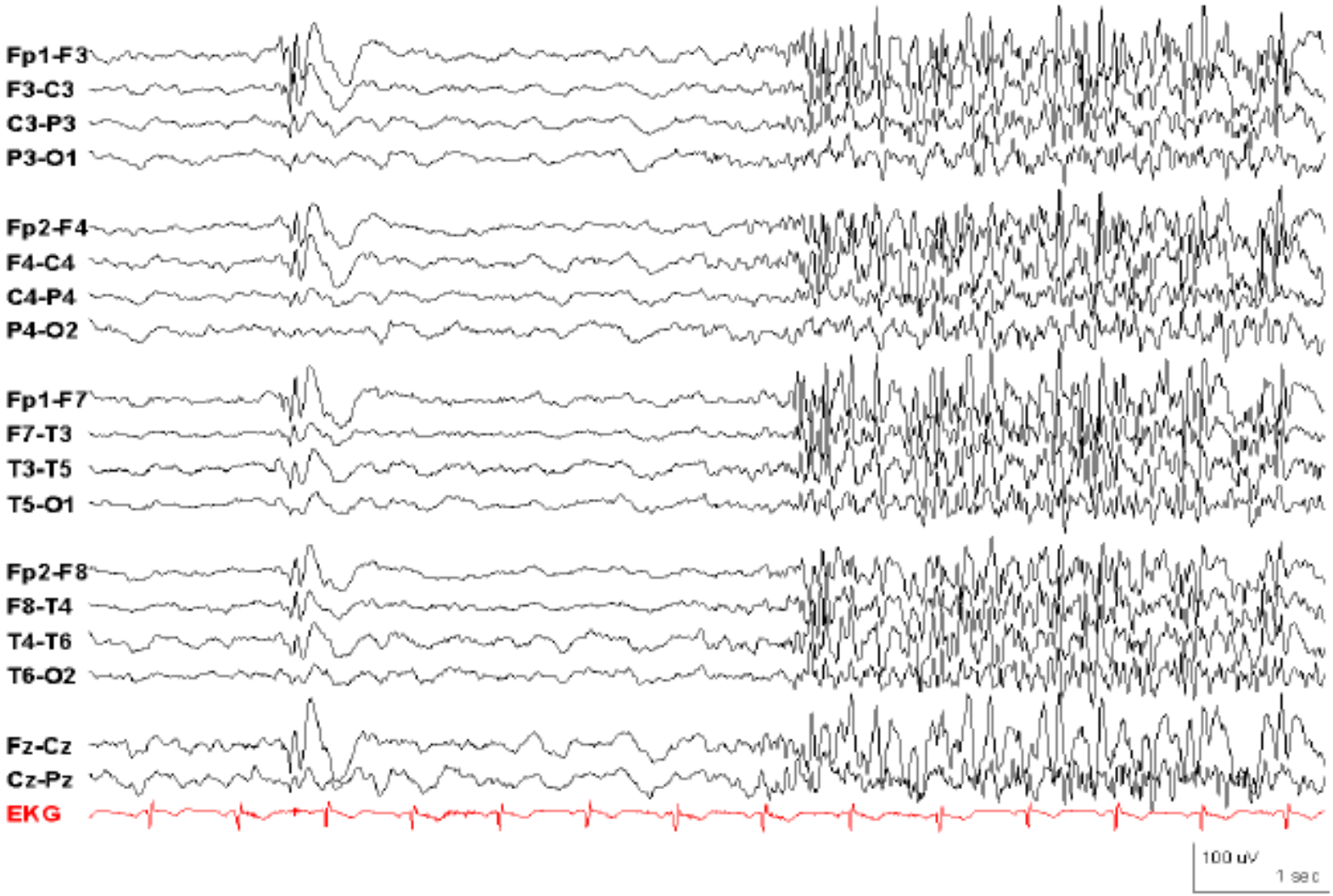
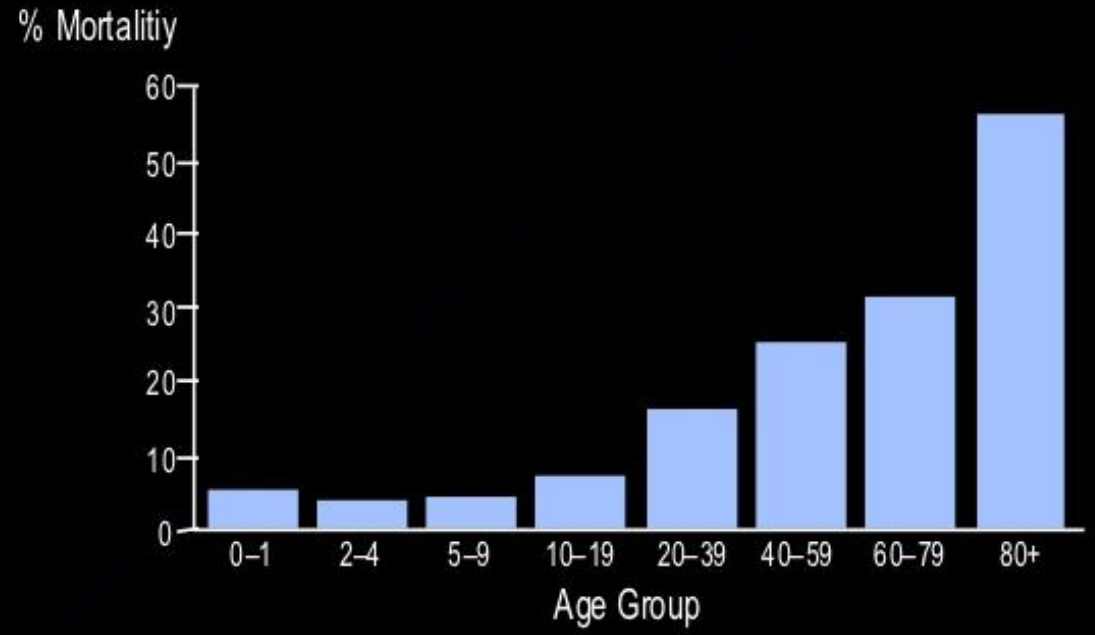

Fp1-F3
F3-C3
C3-P3
P3-O1
Fp2-F4
F4-C4
C4-P4
P4-O2
Fp1-F7
F7-T3
T3-T5
T5-O1
Fp2-F8
F8-T4
T4-T6
T6-O2
Fz-Cz
Cz-Pz
EKG
100 uV
1 sec


FP1-F3
F3-C3
C3-P3
P3-O1
FP2-F4
F4-C4
C4-P4
P4-O2
FP1-F7
F7-T3
T3-T5
T5-O1
FP2-F8
F8-T4
T4-T6
T6-O2
Fz-Cz
Cz-Pz
EKG
75 uV
1 sec

Mortality in Status Epilepticus by Age Group

Among 546 patients with status epilepticus in Richmond, Virginia, from 1982 to 1989.



DeLorenzo RJ, et al. Epilepsia. 1992; 33(suppl 4):515-525.

Complication

Cardiac: HTN,tachycardia,arrhythmia

Pulmonary: apnea,hypoxia,respiratory failure

Hyperthermia

Metabolic derangement

Cerebral:neuronal damage

Death 1-2%

MAJOR THREAT TO LIFE

- Aspiration of gastric contents if the airway is not protected
- Head injury
- Lactic acidosis, hypoxia, hyperthermia, rhabdomyolysis, cerebral edema, or hypotension from a prolonged seizure. These conditions may produce permanent brain injury.
- The patient should be positioned in the *lateral decubitus* position to prevent aspiration of gastric contents. All hard or sharp objects should be removed from the bed.

Table 3. Mortality of SE with Different Etiologies

High Mortality:	Anoxia Multiple medical problems; sepsis
Intermediate Mortality:	[depends on setting, patient population, and follow up] Stroke Tumor Infection (CNS or systemic) Trauma
Low Mortality:	Earlier epilepsy and some precipitant (e.g. reduced AEDs) Medication, drug toxicity Alcohol withdrawal

Summary

Treatment
Step 1

- ABCDE
  - Maintain Airway- patient at risk for aspiration
  - Breathing- place O_2, be ready for intubation
  - Circulation- obtain IV access
  - Dextrose: check glucose levels
  - Electrolytes: check electrolytes (Na, Ca, Mg), and anticonvulsent levels

Treatment Medications

- Ideal drug for treating SE
  - Rapid entry into CNS
  - Rapid onset of action
  - Long duration of action
  - Safety
  - Absence of sedation
  - Useful as maintenance AED

Treatment
Step 2

- Benzodiazepine Therapy
  - Diazepam
  - Lorazepam

Diazepam

- Highly lipid soluble
  - Rapid CNS entry- stops seizures in 1-3 minutes
- Rapid redistribution in fatty tissues
  - Brain concentrations fall quickly
  - Duration of action is 15-30 minutes
  - $T_{1/2}$= 30 hr
- Dose: <3yrs, 0.5mg/kg, >3yrs, 0.3mg/kg
- Side Effects: sedation, decreased respiration and blood pressure

Lorazepam

- Less lipid soluble than diazepam
  - Slower CNS, stops seizures in 6-10 min
- Not as rapidly redistributed to fat stores
  - Longer duration of action 12-24 hr
  - $T_{1/2}$ =14 hr
- Dose: 0.05—0.1mg/kg
- Side Effects: decreased LOC, respiration and BP

Treatment
Step 3

Phenytoin/Fosphenytoin

Phenytoin

- IV dosing 20 mg/kg load
- Stops seizures in 10-30 minutes
- Duration of action 24 hrs, T ½=24hr
- Max infusion rate of 1mg/kg/min, max- 50 mg/min
- Side Effects: arrhythmias, hypotension, wide QT interval, phelibitis
- pH=11-12, may only give IV or po

Treatment
Step 3

Fosphenytoin- phenytoin prodrug

- IV dosing: 20 mg/kg load
- Safer than phenytoin
- pH=8-9
- May give IV or IM
- May give faster than phenytoin(100-150mg/min)
- Much more expensive

Treatment
Step 4

- Phenobarbital
  - Lipid solubility < phenytoin
  - Duration of action>48 hrs, T1/2= 100 hours
  - Dose 20 mg/kg
  - Side Effects: sedation, decreased respiration and BP
  - Be ready to intubate!!

Treatment
Step 5

- If you haven't called Neurology, please call !!!
- Consider IV Valproic Acid (Depacon)
  - FDA approved only for replacement or oral dosing
  - Rapid loading dose appears safe
  - 25-30mg/kg rapidly infused
  - Side Effects: dizziness, HA, nausea

- Consider levetiracetam IV Load

Treatment: Emergent initial therapy

	Strong Recommendations
High or Moderate Quality Evidence	•Benzodiazepines should be given as emergent initial therapy •Lorazepam is the drug of choice for IV administration •Midazolam is the drug of choice for IM administration •Rectal diazepam can be given when there is no IV access and IM administration of midazolam is contraindicated

Treatment: Urgent control therapy

	Strong Recommendations
High or Moderate Quality Evidence	•Urgent control AED therapy recommendations include use of IV fosphenytoin/phenytoin, valproate sodium, or levetiracetam

Brophy, et al NCC 2012

Treatment	Class/Level of evidence
Emergent treatment	
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
Urgent treatment	
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

Brophy, et al NCC 2012

Refractory Status Epilepticus

- Intubation, IV access
- Continuous EEG monitoring
- Medication Coma
  - Pentobarbital
  - Midazolam
  - Propofol

Refractory Status Epilepticus

	Strong Recommendations
Low or Poor Quality Evidence	•Refractory SE therapy recommendations should consist of continuous infusion AEDs, but vary by the patient's underlying condition •Dosing of continuous infusion AEDs for RSE should be titrated to cessation of electrographic seizures or burst suppression •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

Brophy, et al NCC 2012

Treatment	Class/Level of evidence
Refractory treatment	
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

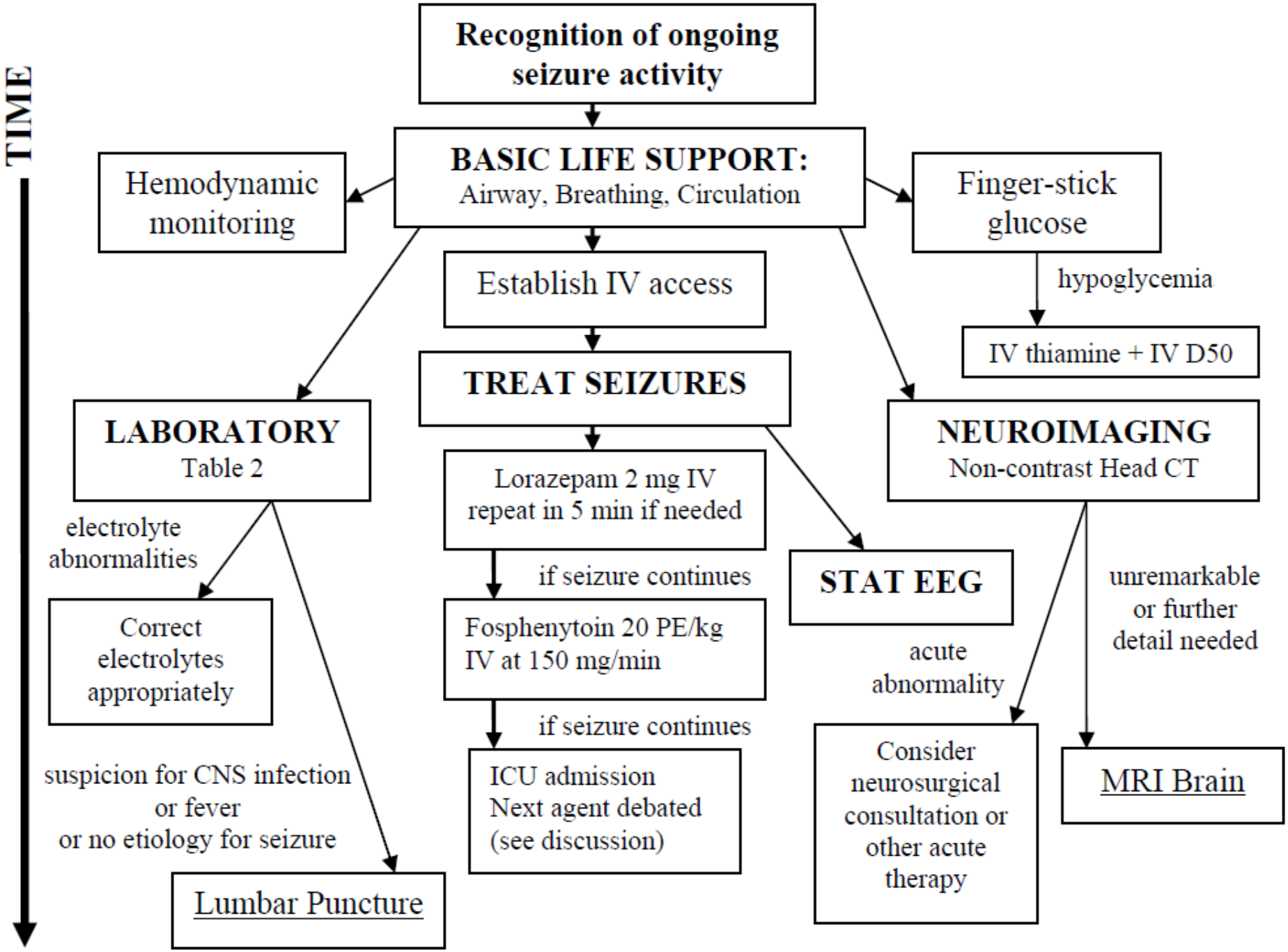
Brophy, et al NCC 2012

Seizure Under control , What next?

Approach: Diagnostic workup

All patients
• FS glucose
• Monitor vital signs.
• Head CT (appropriate for most cases)
• Labs: blood glucose, CBC, BMP, Ca, Mg
• cEEG monitoring
Consider based on clinical presentation
• Brain MRI
• Lumbar puncture
• Toxicology panel (i.e. isoniazid, TCAs, theophylline, cocaine, sympathomimetics, ETOH, organophosphates, cyclosporine)
• Other Labs: LFT, troponin, T&H, coags, ABG, AED levels, tox screen (urine/blood), inborn errors of metabolism

Brophy, et al NCC 2012


TIME
Recognition of ongoing seizure activity
BASIC LIFE SUPPORT:
Airway, Breathing, Circulation
Hemodynamic monitoring
Finger-stick glucose
hypoglycemia
IV thiamine + IV D50
Establish IV access
TREAT SEIZURES
LABORATORY
Table 2
NEUROIMAGING
Non-contrast Head CT
Lorazepam 2 mg IV
repeat in 5 min if needed
if seizure continues
Fosphenytoin 20 PE/kg
IV at 150 mg/min
if seizure continues
ICU admission
Next agent debated
(see discussion)
STAT EEG
electrolyte abnormalities
Correct electrolytes appropriately
suspicion for CNS infection
or fever
or no etiology for seizure
Lumbar Puncture
acute abnormality
Consider neurosurgical consultation or other acute therapy
unremarkable or further detail needed
MRI Brain

Home Messages:

Seizure is a medical emergency.

Don't panic and always keep the protocol in your mind.

Don't hesitate to call the neurology team immediately after you stabilized the patient OR prolonged seizure.

Keep in your mind that seizure is a symptom not a diagnosis .

Thank You