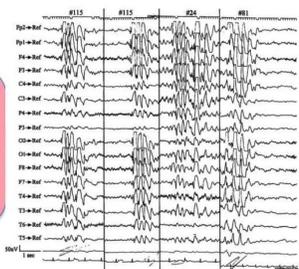
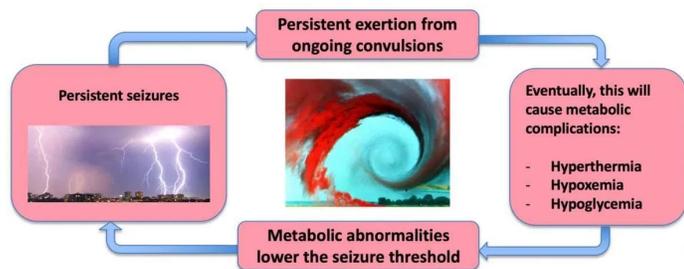


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The Internet Book of Critical Care

Generalized Convulsive Status Epilepticus

February 8, 2020 by **Josh Farkas**



Management of persistent generalized convulsive seizure

1. Assess airway, breathing, and circulation. If resuscitation needed, proceed to #1b.
- 2a. Benzodiazepine after five minutes. Lorazepam 0.1 mg/kg IV up to a max dose of 8 mg. No IV access → 20 mg rectal diazepam. Only have IV diazepam: 10 mg IV q1min, max 30 mg.
- 2b. Order antiepileptic after five minutes. Preferred: levetiracetam 40 mg/kg up to 4,000 mg infused over 10 minutes. Alternative: valproic acid 40 mg/kg (up to 3,000 mg) infused over 5-10 minutes. Give antiepileptic ASAP but do not delay management waiting for antiepileptic.
3. Exclude hypoglycemia. Check finger-stick or give ampic IV glucose.
4. If hyponatremic, treat. 100 mL of 3% NaCl or two ampers of bicarbonate (total 100 mEq in 100 mL).
5. If seizure stops, re-evaluate. Still give levetiracetam or valproate.
6. If seizure continues, prepare for intubation. Preferred induction regimen: 2-3 mg/kg Propofol + 2 mg/kg ketamine + paralytic. Be prepared to manage hypotension (e.g. with norepinephrine infusion & fluid-bolus administration). For patients in shock, replace Propofol with midazolam (total 1.2 mg/kg, infuse 0.1 mg/kg/hr).
7. If still seizing ~10-15 minutes after benzodiazepine, intubate.
8. Start Propofol infusion immediately. Propofol provides ongoing antiepileptic activity. Try to maintain at a rate of 50-80 mg/kg/hr (2.5 mg/kg/hr). May need a norepinephrine or phenylephrine drip to counteract Propofol-induced vasodilation. For unmanageable hypotension, use a midazolam instead of Propofol.

Source: Book of Critical Care, by @EMCrit

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definition of status epilepticus

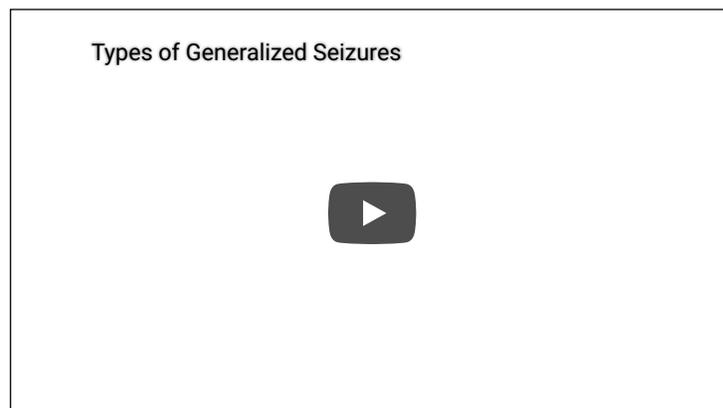
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generalized status epilepticus requires both:

- (1) Generalized seizure: The seizure should cause diffuse motor activity and loss of consciousness. This distinguishes it from a *partial* seizure (e.g. movement of one extremity with retention of consciousness). This is important because partial status epilepticus

("epilepsia partialis continua") can be treated less aggressively.

- (2) Either one of the following:
 - i) A single seizure which lasts for >5 minutes (self-terminating seizures generally last <5 minutes).
 - ii) Multiple seizures without regaining normal mental status in-between.



severity classifications of generalized convulsive status epilepticus

- *Refractory* Status Epilepticus: Refractory to first- and second-line antiepileptic agents.
- *Super-Refractory* Status Epilepticus: Refractory to two anti-epileptic agents and general anesthesia treatment for 24 hours.
 - More likely to be due to acute encephalitis (30516601).

epilepsia partialis continua

- This involves ongoing *partial, focal* seizures (e.g. twitching of a single extremity).
- This is generally *not* life-threatening, as it doesn't affect consciousness or airway protection. It can persist for months or years.
- Treatment is extremely challenging, with seizures often being refractory to multiple medications. Some restraint may be needed, as the treatment may be more dangerous than the disease itself.

differentiation from pseudoseizure

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pseudoseizure (technical terminology: "Paroxysmal Non-Epileptic Seizures")

- Clinical phenomenon which mimics a seizure, often related to psychiatric stress.
- Patients are *not* aware that this isn't a real seizure (they aren't "faking it").
- Can occur in patients with epilepsy, creating a very confusing picture (patients can have episodes of both genuine seizures and pseudoseizures).

clinical clues to pseudoseizure

- Movement of all extremities with preservation of consciousness (e.g. speaking).
- Eyes that are squeezed shut (true generalized status epilepticus patients should be unconscious and *not* resist eyelid raising).
- Responsiveness to noxious stimuli (e.g. nasal swab for influenza).
- Out-of-phase movement of limbs (in true generalized seizure, the limbs generally move synchronously).
- Unusual movements (e.g. pelvic thrusting, side-to-side head movement).
- Optokinetic nystagmus: viewing an optokinetic drum or video (example below) will elicit nystagmus.



evaluation and management

- When in doubt, video EEG capture can help make these distinctions.
- If a diagnosis can't be made with certainty, the safest approach can be to treat these as genuine seizures (e.g. with benzodiazepine).

causes

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Many factors often *combine* to lower the patient's seizure threshold, leading to status epilepticus. Ideally, all such factors will be addressed, reducing the likelihood of recurrence.

metabolic

- Hyponatremia/hyponatremia
- Hypoglycemia/hyperglycemia (hyperglycemia may tend to cause focal seizures)
- Hypophosphatemia
- Hypoxemia, respiratory alkalosis
- Uremia, dialysis disequilibrium
- Hyperammonemia (of any cause), hepatic encephalopathy
- Hyperthermia

malignancy

- Primary brain tumor (e.g. glioblastoma multiforme)
- Metastatic disease

infectious / inflammatory

- Meningitis, encephalitis (viral, paraneoplastic, anti-NMDA receptor encephalitis)
- Brain abscess
- Lupus, vasculitis
- Sepsis with systemic inflammation (may reduce seizure threshold)

vascular

- Remote stroke which caused residual epileptogenic focus.
- Acute stroke (ischemic > hemorrhagic).
- Hypertension-related:
 - Hypertensive encephalopathy /Posterior Reversible Encephalopathy Syndrome (PRES)
 - Eclampsia

traumatic brain injury

drugs

- (1) Non-adherence with anti-epileptic therapy, changes in regimen, drug-drug interactions
- (2) Medications that lower seizure threshold; more common examples:
 - Psychiatric medications (antipsychotics; antidepressants, especially bupropion or tricyclics; lithium)
 - Local anesthetics (e.g. lidocaine)
 - Antimicrobials (e.g. beta-lactams, quinolones, metronidazole, acyclovir, gancyclovir, isoniazid)
 - Antihistamines, baclofen
 - Ancient analgesics (tramadol, meperidine, propoxyphene)
 - Chemotherapeutics & immunomodulators (e.g. cisplatin, methotrexate, tacrolimus, cyclosporine)
 - Theophylline
 - *Withdrawal* of benzodiazepines, barbiturates, baclofen, or gabapentin.
- (3) Toxicologic
 - Withdrawal from alcohol or benzodiazepine
 - Overdose with sympathomimetic, salicylate, tricyclic, anticholinergic, lithium, synthetic cannabinoids

status epilepticus without an obvious cause? think **NORSE**

NORSE (new-onset refractory status epilepticus)

- Definition: Refractory status epilepticus without any readily identifiable cause (in a patient without prior seizures or structural neurologic disease).
- Causes:
 - ~40% Non-paraneoplastic autoimmune (e.g. anti-NMDA encephalitis)
 - ~30% Paraneoplastic
 - ~20% Infectious

investigation

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history

- Careful review of medication list, including any recent changes (look up drugs individually to determine if they lower seizure threshold).
- ? Preceding febrile illness or other complaints.
- ? Use of alcohol or other substances.
- ? Seizure initiated with *focal* symptoms, with subsequent generalization (this suggests focal neurologic pathology).

neuro exam

- Immediately following the seizure, patients may have focal neurologic defects in areas involved in the seizure (Todd's Paralysis).
- Prompt examination is important, as findings may disappear over time.
- A *focal* abnormality on neurologic examination (e.g. asymmetric findings) suggests a *focal* neurologic lesion as the trigger of the seizure. This increases the importance of neuroimaging.

labs

- Basics
 - Fingerstick glucose (should be done immediately).
 - CBC, chemistries including Ca/Mg/Phos.
 - Liver function tests, including ammonia level.
 - Creatinine kinase (to evaluate for rhabdomyolysis due to seizures).
 - Urinalysis, urine pregnancy test if relevant.
- Additional considerations
 - Anti-epileptic drug levels (usually not available rapidly, but may be helpful later on to differentiate between nonadherence and medication failure).
 - Toxicology workup as indicated (e.g. urine toxicology screen including cocaine and methamphetamine).

neuroimaging

- CT head generally indicated unless cause is obvious (e.g. non-adherence with anti-epileptic agents).
- MRI useful if etiology remains unclear.

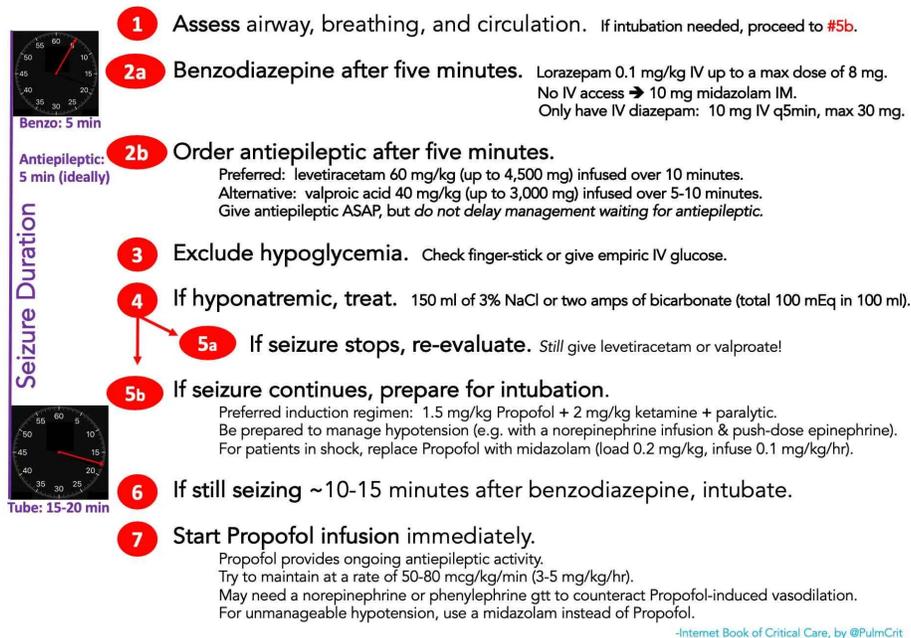
lumbar puncture

- The main indication is usually exclusion of meningitis/encephalitis, if this is suspected clinically.
- Note that prolonged status epilepticus itself can cause elevation of protein and total cell count (but not above ~80-100 /mm³).

treatment algorithm

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Management of persistent generalized convulsive seizure



This algorithm describes the approach to a convulsive generalized seizure lasting >5 minutes. For a patient with recurrent seizures who isn't actively seizing, a more gradual approach may be taken (with escalation if an active seizure resumes).

The duration of time in which a patient can be in convulsive status epilepticus before brain damage occurs is unknown. Many experts estimate this to be around 30 minutes (30516601). Consequently, the above algorithm is designed to break nearly all seizures within 30 minutes. This requires rapid escalation to intubation.

benzodiazepine is front-line therapy

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dosing

- **IV lorazepam** is generally the preferred agent.
 - The best research supports a dose of **0.1 mg/kg lorazepam IV** ([Treiman 1998 \(https://www.ncbi.nlm.nih.gov/pubmed/9738086\)](https://www.ncbi.nlm.nih.gov/pubmed/9738086)).
 - However, many guidelines recommend giving 4 mg IV initially, with a repeat dose if this isn't effective. That may also be reasonable.
- For patients without IV access, give **10 mg intramuscular midazolam** ([Silbergieit 2011 \(https://www.ncbi.nlm.nih.gov/pubmed/21967361\)](https://www.ncbi.nlm.nih.gov/pubmed/21967361)).
- Diazepam: 10 mg IV, may repeat q5-10 minutes to a maximum cumulative dose of 30 mg.

do not under-dose your benzodiazepine

- Over time, GABA receptors on neurons are internalized within cells. This reduces the sensitivity of the seizure to benzodiazepines.
- Up-front adequate dosing of benzodiazepine provides the best chance for immediate lysis of the seizure.

- Evidence does NOT support the concept that benzodiazepines for status epilepticus promote respiratory depression and intubation. In fact, adequate doses of benzodiazepines may *reduce* the need for intubation. One caveat here is that the clinician must be *patient* in allowing the postictal, post-benzodiazepine patient to wake up (these patients *will* have altered mental status, but by itself that's not an indication for intubation).

don't stop here!

- Even if the benzodiazepine breaks the seizure, you still need to give the patient a conventional anti-epileptic agent! More on this below.

hypoglycemia & hyponatremia

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exclude hypoglycemia

- Hypoglycemia must be excluded in any patient with seizures or mental status changes.
- Usually a finger stick-glucose is adequate for this. However, if there is difficulty obtaining a finger-stick glucose or if the measurement is borderline, just give IV glucose empirically (1-2 ampules of D50W).

treat hyponatremia if present

- Hyponatremia is an uncommon cause of seizures. However, this is important because seizures due to hyponatremia should be treated with hypertonic saline immediately.
- Standard therapy would be a bolus of 150 ml 3% saline, which may be repeated once for ongoing seizure.
- Hypertonic saline often takes 15-20 minutes to arrive from pharmacy. In an emergency, 2 amps of bicarbonate (each amp equals 50 mEq bicarbonate in 50 ml) can be substituted for 150 ml of 3% saline (described further [here \(https://emcrit.org/pulmcrit/emergent-treatment-of-hyponatremia-or-elevated-icp-with-bicarb-ampules/\)](https://emcrit.org/pulmcrit/emergent-treatment-of-hyponatremia-or-elevated-icp-with-bicarb-ampules/)).

conventional anti-epileptic

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conventional anti-epileptic agent is indicated for ALL status epilepticus patients

- Any patient who seizes for >5 minutes should receive an anti-epileptic agent, even if benzodiazepine is successful in stopping the seizure. The benzodiazepine will last only for a few hours, so treatment with benzodiazepine alone leaves the patient at risk for delayed seizure recurrence.
- There is no reason to intentionally delay the conventional anti-epileptic agent until after the benzodiazepine (because it will be required regardless).
- For a patient with active convulsive seizures, don't delay intubation while waiting for the anti-epileptic agent to arrive from the pharmacy.
 - The anti-epileptic should be ordered ASAP and given as early as possible.
 - If the anti-epileptic arrives from pharmacy and breaks the seizure within 20 minutes then intubation isn't necessary. That would be terrific, but in most scenarios this is logistically impossible.
 - Intubation shouldn't be delayed while waiting to see if the second-line antiepileptic agent will work (target intubation by ~20 minutes after seizure initiation, regardless of whether or not the conventional anti-epileptic agent has arrived).

levetiracetam is the generally the preferred agent

- Benefits of levetiracetam:
 - It has essentially no contraindications – so you can safely prescribe this to patients without knowing much about them.
 - It can be infused rapidly.
 - It is extremely safe; in particular, it is unlikely to cause alteration in consciousness (31766004).
 - It has minimal interactions with other drugs.
- Contraindications: None
- Side-effects: Can cause mood disturbance, SIADH
- Dosing
 - Loading dose: 60 mg/kg up to a max total dose of 4.5 grams, infused over 10 minutes.

- Maintenance dose: usually 1-1.5 grams IV q12hr (up to 2 grams IV q12 hr in selected cases).

valproic acid

- A reasonable option
- Contraindications
 - Hyperammonemia, liver disease
 - Pregnancy
 - Thrombocytopenia, active bleeding
- Side-effects
 - Thrombocytopenia, impaired platelet aggregation
 - Pancreatitis, hepatotoxicity
 - Hyperammonemic encephalopathy
 - Stevens-Johnson Syndrome
 - Drug reaction with eosinophilia and systemic symptoms (DRESS)
 - SIADH
- Dosing
 - Loading dose: 40 mg/kg (up to 3,000 mg) infused over 5-10 minutes. May give additional 20 mg/kg over 5 minutes.
 - Maintenance dose: 30-60 mg/kg daily in divided doses, q12hr or q8hr.
- Monitoring
 - Target serum level 80-140 mg/dL.
 - Target free level of 4-11 ug/ml (obtain free level only if toxicity is suspected).

fosphenytoin

- *Reasons fosphenytoin isn't generally preferred.*
 - It has numerous contraindications (e.g. pregnancy, hepatic dysfunction, renal dysfunction).
 - It can cause bradycardia or hypotension (if given too rapidly, or to patients with cardiac comorbidity). Other potential complications include Stevens-Johnson Syndrome, pancytopenia, tissue necrosis if extravasation occurs, phlebitis, and drug fever.
 - It causes numerous drug-drug interactions. In particular, it shouldn't be used together with valproate (valproate inhibits CYP2C9, which leads to accumulation of phenytoin; valproate also competes for binding to albumin and thereby increases the free level of phenytoin).
 - Monitoring phenytoin levels in the ICU is often impossible (unless your lab provides rapid turn-around time on free phenytoin levels).
 - Toxic levels may cause delirium.
- Dosing
 - Loading dose is 20 PE/kg at 100-150 PE/min (may give additional 5-10 PE/kg for ongoing seizures). Fosphenytoin is dosed in terms of "fosphenytoin equivalents" rather than mg.
 - Maintenance dose is 5-7 PE/kg/day in 2-3 divided doses.
- Monitoring
 - Target total level of ~15-25 ug/mL (but this isn't very accurate for critically ill patients). This may be corrected for albumin if free fosphenytoin levels aren't rapidly available (online calculator [here \(https://clincalc.com/Phenytoin/Correction.aspx\)](https://clincalc.com/Phenytoin/Correction.aspx)).
 - Ideally, a *free* phenytoin level may be checked, targeting a level of 2-3 ug/mL (especially in patients with renal dysfunction or other medications which compete with phenytoin for albumin binding).
 - Check levels at least >2 hours after the last dose.

phenobarbital

- Not widely used, but may be helpful in specific situations:
 - (1) Arguably the *preferred* anti-epileptic for alcohol withdrawal seizures. More on this [here \(https://emcrit.org/ibcc/etoh/#alcohol_withdrawal_seizures\)](https://emcrit.org/ibcc/etoh/#alcohol_withdrawal_seizures).
 - (2) May be useful in super-refractory status epilepticus, to assist in weaning patients off a barbiturate coma.

loading dose for patients on chronic anti-epileptic therapy

- All patients with status epilepticus should be loaded with an anti-epileptic agent (usually levetiracetam, fosphenytoin, or valproate).
- For patients on one of these drugs previously:

- If the patient is believed to be adherent with therapy, it could make sense to load with a *different* drug. For example, a valproate load could be used in a patient on chronic levetiracetam.
- If the patient is felt to be potentially non-adherent, then re-loading with the patient's chronic anti-epileptic could make sense.
- When in doubt, levetiracetam may be a good choice here, because supra-therapeutic levels are reasonably safe.

neurolytic intubation

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preparation for intubation

- Propofol is generally the best induction drug here, given its potent anti-epileptic activity. The only exception would be a patient with severe hypotension (in whom midazolam provides more hemodynamic stability). Ketamine has anti-epileptic activity as well, which may function synergistically with propofol or midazolam (ketamine blocks NMDA receptors, while propofol blocks GABA receptors).
- The combination of sedation, vasodilation from propofol, and positive pressure ventilation may decrease the blood pressure. Be prepared for this (e.g. have a norepinephrine infusion and/or push-dose epinephrine ready).
- Regarding paralytic:
 - Succinylcholine may be contraindicated in prolonged status epilepticus, as this may lead to rhabdomyolysis and *hyperkalemia*.
 - Rocuronium causes prolonged paralysis, which may be problematic because it can mask ongoing seizure activity. However, sugammadex can be used following intubation to reverse paralysis and determine if there is residual seizure activity (if EEG isn't readily available).
 - Note that muscular paralysis won't prevent brain damage from ongoing seizure activity. The goal is always to control the seizure itself, *not* to mask it using paralytics.
 - Placement of a tourniquet on an extremity before paralysis may prevent paralytic from entering that extremity, thereby allowing you to determine if the seizure has been terminated.

example of a neurolytic intubation

- There are many ways to accomplish this. One strategy involves the following sequence of drugs:
 - #1: Push 200 mg IV ketamine.
 - #2: Push 100 mg of propofol (10 ml).
 - #3: Push 0.6 mg/kg rocuronium (this is a *lower* dose than is usually used, so that it will take a bit *longer* to work than usual and won't last too long).
- This will result in one of two outcomes:
 - (#1) The ketamine and propofol will usually break the seizure. This results in an *abrupt* cessation of motor activity about 30-60 seconds after pushing the propofol (before the onset of paralysis). You can usually intubate the patient when that occurs – the patient is generally quite flaccid.
 - (#2) The ketamine and propofol *fail* to break the seizure. In this case, seizure movements will *gradually* become less pronounced as paralysis occurs. Disappearance of all movement generally occurs >60 seconds after administration of rocuronium.
- Based on the dose and sequence of drugs used, the rocuronium isn't generally really needed here (the propofol and ketamine will generally break the seizure and produce adequate intubating conditions). The rocuronium is merely an insurance policy so that in case the propofol and ketamine *don't* break the seizure, you will still get adequate intubating conditions.

initiate sedative infusion (propofol)

- Propofol (+/- ketamine) will generally break the seizure. However, an ongoing infusion of propofol is still needed to prevent seizure recurrence.
- If possible, **propofol** should be infused at a moderate-high rate (e.g. 50-80 mcg/kg/min). A low dose of vasopressor may be needed to allow for propofol administration. [Phenylephrine](https://emcrit.org/pulmcrit/phenylephrine-epinephrine-central-access/) (https://emcrit.org/pulmcrit/phenylephrine-epinephrine-central-access/) may be preferable here for patients without central access.
- For severely hypotensive patients, a midazolam infusion may be used instead of propofol. The main drawback of midazolam is that it accumulates and wears off slowly, delaying extubation.

super-refractory status epilepticus

Rarely, seizures may fail to respond to a traditional anti-epileptic agent (e.g. levetiracetam) plus propofol infusion. This is a largely evidence-free zone, given its rarity. Additional treatment options include the following.

re-bolus with propofol and ketamine

- Sometimes merely re-bolusing with propofol and ketamine will break the seizure and settle things down.
- Ensure that the propofol infusion dose is adequate (hemodynamic instability caused by propofol may be managed by norepinephrine if necessary, and ideally should not be a barrier to using adequate doses of propofol).
- This isn't a long-term solution, but may help break the seizure. It may be used in conjunction with some of the below techniques to help prevent seizure recurrence.

additional conventional anti-epileptic agents

- A second conventional agent may be added on (including valproic acid, levetiracetam, or fosphenytoin).
- These agents are not necessarily intended to *break* the seizure immediately, but rather to assist in ongoing seizure control (as infused sedatives are weaned).

other adjunctive anti-epileptic agents

- lacosamide
 - A newer anti-epileptic agent, which is generally well tolerated and easy to use.
 - A reasonable loading dose may be 400 mg over 5 minutes, followed by maintenance doses of 200 mg IV q12hr.
- topiramate
 - Loading dose of 300-800 mg, followed by a daily dose of 200-500 mg BID (31766004).
 - Affects several receptor systems (GABA, calcium channel inhibition, sodium channel blockade, AMPA/kainate receptor inhibition).
- pyridoxine (vitamin B6)
 - This may be more useful in specific types (INH poisoning, alcoholism, some pyridoxine metabolism deficiencies).
 - The dose is 100-600 mg/day either PO or IV.

high-dose ketamine infusion

- This is emerging as a preferred agent to control super-refractory status epilepticus.
- Advantages compared to barbiturate coma:
 - i) More hemodynamically stable
 - ii) Shorter half-life
 - iii) Can be rapidly up-titrated to determine efficacy (and, if not working, another agent may be used).
- Dosing
 - (1) *Ketamine Titration Challenge*: Give successive boluses of 1-2 mg/kg every 5 minutes, up to a total of 5-10 mg/kg max cumulative dose. If this *succeeds* in controlling the seizure, then proceed to a maintenance infusion. If this *doesn't* control the seizure, then try a different agent (e.g. pentobarbital below).
 - (2) Maintenance infusion: The infusion dose range is roughly 1-10 mg/kg/hr.
 - Titrate based on EEG.
 - For break-through seizures, may bolus with ketamine and increase the infusion rate.

pentobarbital

- Last-line agent for super-refractory status epilepticus.
- Pentobarbital is almost uniformly effective. However, the problem is that it has many side-effects (including hypotension, propylene glycol toxicity) and an incredibly sluggish half-life. Thus, putting a patient into a pentobarbital coma commits them to a 1-2 week ventilator course.
 - Withdrawal of life-sustaining therapy subsequent to induction of a pentobarbital coma is ethically questionable. Ideally, pentobarbital should be reserved for patients who are committed to aggressive support. If families wish to trial a short course of intubation (e.g. 1-2 days), then a ketamine infusion would be more appropriate.
 - In a small RCT of propofol versus barbiturates, there was a similar rate of seizure control, but patients treated with barbiturates had a substantially longer duration of mechanical ventilation (20878265).

- Dose
 - Loading dose is 5-15 mg/kg. Repeat doses of 5 mg/kg until the seizure stops.
 - Infusion rate: start at 1 mg/kg/hr, then titrate between 0.5-10 mg/kg/hr.

ketogenic diet

- This may be effective, even for super-refractory status epilepticus (24453083, 30638692).
- This is extremely safe (the risk/benefit ratio is arguably superior to most anti-epileptic agents).
 - Nutritional ketosis be done in patients with Type-I diabetes, although is more complicated and requires closer monitoring.
 - It is contraindicated in patients with certain mitochondrial disorders.
- Main barriers are logistic:
 - Ketogenic tube feed formulation is required (many hospitals may lack this).
 - Drugs formulated in D5W must be avoided.

neuromonitoring

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clinical monitoring

- If patients can regain normal consciousness, they aren't seizing.
- An inability to regain consciousness raises concern for persistent non-convulsive status epilepticus (NCSE).

video EEG (vEEG)

- Continuous vEEG is preferred (especially for more complex patients). For patients who don't regain normal consciousness, intermittent seizures may be occurring which could be missed with a single "spot" EEG.
- There is no consensus or data regarding whether it is best to titrate medication to target burst-suppression or simply the absence of seizures.
 - Targeting a deeper level of sedation (e.g. burst-suppression) will generally increase time on ventilation and medication-related complications.
 - In the absence of clear evidence, simply targeting the absence of seizures may minimize iatrogenic harm.
- vEEG can lead to over-treatment and iatrogenic harm, *if*.
 - (1) A decision is made to target burst-suppression or flat-line EEG for prolonged periods of time.
 - (2) Efforts are made to suppress *all* ictal-spectrum patterns (e.g. periodic lateralizing epileptiform discharges).

waking & weaning

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basic considerations prior to extubation

- (1) Have all causes of the seizure been addressed?
- (2) Are any further diagnostic tests needed?
 - MRI is easier and safer to do when intubated; after intubation patients will often not be able to lie still enough for MRI.
 - LP is easier to perform prior to extubation.
- (3) Have adequate doses of anti-epileptic medications been given?

extubation

- Once the above criteria have been met, sedation can be lifted.
- Most patients will be kept intubated at least one day. For very refractory seizures, a longer period of sedation may be needed.
- Careful monitoring is required to determine if there are any ongoing seizures. Subsequently, the patients may be extubated if they meet other criteria (e.g. they pass a spontaneous breathing trial).

summary

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Management of persistent generalized convulsive seizure

- 1** Assess airway, breathing, and circulation. If intubation needed, proceed to #5b.
- 2a** Benzodiazepine after five minutes. Lorazepam 0.1 mg/kg IV up to a max dose of 8 mg. No IV access → 10 mg midazolam IM. Only have IV diazepam: 10 mg IV q5min, max 30 mg.
- 2b** Order antiepileptic after five minutes. Preferred: levetiracetam 60 mg/kg (up to 4,500 mg) infused over 10 minutes. Alternative: valproic acid 40 mg/kg (up to 3,000 mg) infused over 5-10 minutes. Give antiepileptic ASAP, but do not delay management waiting for antiepileptic.
- 3** Exclude hypoglycemia. Check finger-stick or give empiric IV glucose.
- 4** If hyponatremic, treat. 150 ml of 3% NaCl or two amps of bicarbonate (total 100 mEq in 100 ml).
- 5a** If seizure stops, re-evaluate. Still give levetiracetam or valproate!
- 5b** If seizure continues, prepare for intubation. Preferred induction regimen: 1.5 mg/kg Propofol + 2 mg/kg ketamine + paralytic. Be prepared to manage hypotension (e.g. with a norepinephrine infusion & push-dose epinephrine). For patients in shock, replace Propofol with midazolam (load 0.2 mg/kg, infuse 0.1 mg/kg/hr).
- 6** If still seizing ~10-15 minutes after benzodiazepine, intubate.
- 7** Start Propofol infusion immediately. Propofol provides ongoing antiepileptic activity. Try to maintain at a rate of 50-80 mcg/kg/min (3-5 mg/kg/hr). May need a norepinephrine or phenylephrine gtt to counteract Propofol-induced vasodilation. For unmanageable hypotension, use a midazolam instead of Propofol.

-Internet Book of Critical Care, by @PulmCrit

Guide to anti-epileptic agents

Medication	Dose	Contraindications	Side effects	Notes
First-line Agents = Benzodiazepines				
Lorazepam	0.1 mg/kg IV (ideal body weight)	<i>Please note that immediate administration of adequate doses of benzodiazepine is probably the most important intervention for status epilepticus. BZDs don't cause respiratory suppression here - they cause recovery.</i>		Best agent if IV access.
Midazolam	10 mg IM			Front-line if no IV access.
Diazepam	10 mg IV, may repeat q5 min x3			Rapidly re-distributes into adipose; efficacy short-lived.
"Standard" Second-line Agents				
Levetiracetam	Load: 60 mg/kg up to 4.5 grams over 10 min. Maintenance: 1 - 1.5 grams q12hr Renally cleared: dose adjust in renal failure.	None	SIADH Mood disturbance	
Valproic acid	Load: 40 mg/kg up to 3000 mg, over 5-10 min. May add 20 mg/kg over 5 min. Maintenance: 30-60 mg/kg daily, divided TID.	Hyperammonemia, liver disease Urea cycle or mitochondrial dz Pregnancy Thrombocytopenia, bleeding	Hyperammonemia, encephalopathy Stevens-Johnson syndrome Drug rxn w/ eosinophilia & systemic sx SIADH Pancreatitis, hepatotoxicity Thrombocytopenia	Target serum level 80-140 mg/dL. Avoid combination with fosphenytoin.
Fosphenytoin	Load 20 PE/kg at 100-150 PE/min. May add 5-10 PE/kg for persistent seizures (PE = phenytoin equivalents). Maintenance: 5-7 PE/kg/day in 2-3 divided doses.	Pregnancy Hepatic or renal dysfunction Hypotension, bradycardia. Seizures due to cocaine, local anesthetics, lindane, or theophylline (tox seizures).	Hypotension, bradycardia Stevens-Johnson syndrome Pancytopenia Delirium Numerous drug-drug interactions	Avoid combination with valproate.
Phenobarbital	Load: 15-20 mg/kg at 50 mg/min. Additional doses may be added for max total dose of 30 mg/kg. Maintenance: ~60-100 mg BID	Porphyria Prior chronic phenobarbital use.	Somnolence, respiratory suppression. Long half-life may increase risk of prolonged sedation.	Arguably front-line agent for alcohol withdrawal seizures. Usual therapeutic target is 15-40 ug/ml.
Add-on Agents				
Lacosamide	Load: 400 mg IV over 5 minutes Maintenance: 200 mg IV q12hr	Pre-existing heart block or conduction system disease.	Atrioventricular block Hypotension	Newer agent. Safe, minimal drug interactions.
Topiramate	Load: 300-800 mg PO Maintenance: 200-500 mg BID PO		Renal tubular acidosis	No IV form
Thiamine (vitamin B1)	If concern for Wernicke's: 500 mg IV q8hr To prevent Wernicke's: 100 mg IV daily	None	None	Traditional component of status epilepticus management. Thiamine deficiency doesn't usually manifest with seizure, but this is possible.
Pyridoxine (vitamin B6)	100-600 mg daily (PO or IV)	None	None	Most useful in: INH poisoning, alcoholism/malnutrition, chronically critically ill. Safe, may help some patients.
Agents for continuous IV infusion				
Propofol	Load: 2 mcg/kg. May repeat if hemodynamically tolerated to total 10 mg/kg. Infuse: 30-200 mcg/kg/min (Avoid >83 mcg/kg/min for long periods)	Hemodynamic instability Hypertriglyceridemia	Hypotension, occasional bradycardia Hypertriglyceridemia Propofol infusion syndrome	Preferred agent, easy to titrate. If abruptly stopped, patients may have rebound seizure.
Ketamine	Load: 1-2 mg/kg. May repeat to max 10 mg/kg. Infuse: 1-8 mg/kg/hr		May increase Bp & heart rate. May exhaust ketamine supply.	Under-appreciated as an anti-epileptic. Combines nicely with Propofol (Propofol inhibits GABA, ketamine inhibits glutamate).
Midazolam	Load: 0.2 mg/kg. May repeat q5-10 up to 2 mg/kg total dose. Infuse: 0.05-2 mg/kg/hr		Delirium, drug accumulation leading to delayed extubation (although to a lesser extent than pentobarbital).	Accumulates over time, causing longer half-life. Ongoing use causes resistance (tachyphylaxis).
Pentobarbital	Load: 5-15 mg/kg. May repeat 5 mg/kg doses until seizure lyses. Infuse: 0.5-5 mg/kg/hr	Hemodynamic instability Porphyria	Hypotension Ileus Persistent coma (half-life is 15-60 hr!)	Very sluggish agent, obligates patient to prolonged intubation and long ICU stay. Target serum level 30-45 ug/mL.

podcast

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(<https://i1.wp.com/emcrit.org/wp-content/uploads/2016/11/apps.40518.14127333176902609.7be7b901-15fe-4c27-863c-7c0dbfc26c5c.5c278f58-912b-4af9-88f8-a65fff2da477.jpg>)

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questions & discussion

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To keep this page small and fast, questions & discussion about this post can be found on another page [here \(https://emcrit.org/emcrit/status-epilepticus-3/\)](https://emcrit.org/emcrit/status-epilepticus-3/).



(<https://i0.wp.com/emcrit.org/wp-content/uploads/2016/11/pitfalls2.gif>)

- Avoid leaving the bedside of a patient in generalized convulsive status epilepticus until the seizures are controlled. This should nearly always be possible within <30 minutes (using intubation and high-dose ketamine if necessary).
- ALL patients with status epilepticus should be treated with a conventional anti-epileptic agent (e.g. levetiracetam), regardless of whether the seizure responds to benzodiazepine. If the benzodiazepine works, you still need to follow up with an anti-epileptic agent for longer term efficacy.
- Avoid inadequate dosing of levetiracetam (recent guidelines recommend 60 mg/kg, up to 4.5 grams).
- Avoid inadequate dosing of benzodiazepine up-front (0.1 mg/kg might be ideal; anything below 4 mg lorazepam is woefully inadequate).
- Beware of using paralytic for intubated patients with convulsive seizure – this makes things look nice but doesn't prevent brain damage from the seizure.
- Don't fall prey to *intubatophobia*: the fear that intubating seizure patients may make them worse. On the contrary, early airway management facilitates definitive seizure control and prevents complications (e.g. aspiration, rhabdomyolysis).

Going further:

- PulmCrit
 - [Rapid-sequence termination \(2014\) \(https://emcrit.org/pulmcrit/rapid-sequence-termination-rst-of-status-epilepticus/\)](https://emcrit.org/pulmcrit/rapid-sequence-termination-rst-of-status-epilepticus/)
 - [Resuscitator's guide to status \(https://emcrit.org/pulmcrit/status-epilepticus-2/\)](https://emcrit.org/pulmcrit/status-epilepticus-2/)
 - [All conventional 2nd line anti-epileptics are equally bad: ESETT trial \(https://emcrit.org/pulmcrit/esett/\)](https://emcrit.org/pulmcrit/esett/)
- [EMCrit podcast #155: Status epilepticus with Tom Bleck \(https://emcrit.org/podcasts/status-epilepticus/\)](https://emcrit.org/podcasts/status-epilepticus/)
- [Status Epilepticus \(https://first10em.com/status-epilepticus-update/\)](https://first10em.com/status-epilepticus-update/) (First10EM, Justin Morgenstern)
- [Status Epilepticus \(https://emergencymedicinecases.com/status-epilepticus/\)](https://emergencymedicinecases.com/status-epilepticus/) (EMCases, Anton Helman)
- [Status Epilepticus \(https://litfl.com/status-epilepticus/\)](https://litfl.com/status-epilepticus/) (LITFL, Chris Nickson)

The Internet Book of Critical Care is an online textbook written by Josh Farkas (@PulmCrit), an associate professor of Pulmonary and Critical Care Medicine at the University of Vermont.

