Status epilepticus

Dr FL Chow
Terms

• **Seizure** – paroxysmal event due to abnormal excessive neuronal activity in brain
• **Epilepsy** – recurrent seizures due to chronic, underlying process; epilepsy syndromes
• Classification of seizures – diagnosis, therapy, prognosis
• International League against Epilepsy (ILAE) – clinical features and EEG
Classification of seizures

- Focal – motor, sensory, autonomic, cognitive
- Generalized – absence, tonic-clonic, clonic, tonic, atonic, myoclonic
- Unclear
# Classification

## Focal seizures
- Arise from neuronal network in one hemisphere
- Spread of activity (movement)
- Paresis
- Continue for hours or days
- Auras
- Dyscognitive features
- Secondary generalization
- Interictal EEG may be normal or show epileptiform spikes or sharp waves

## Generalized seizures
- Engage neuronal network in both cerebral hemispheres
- **Generalized tonic-clonic** – most common type from metabolic derangement, EEG polyspikes, spike – wave, slow
- Typical absence (spike – wave)
- Atypical absence
- Atonic
- Myoclonic
Causes of seizures and epilepsy

• Shift in balance of excitation and inhibition in CNS

• Normal brain have seizure under appropriate circumstances (endogenous factor, genetic)

• Condition and process of epileptogenesis (trauma, stroke, infection): hyperexcitable neuron network

• Precipitating factors (physiological, physical, exogenous such as toxic substance)

• Age (febrile illness, epilepsy syndromes, acquired CNS lesions, cerebrovascular diseases, metabolic)
Seizure development

• Seizure initiation
  – high frequency bursts of action potentials and hyper-synchronization
  – influx of extracellular Ca\(^{2+}\) → opening of voltage gated Na\(^{+}\) channels → influx of Na\(^{+}\) → generation of repetitive action potentials → hyperpolarizing after potential by GABA receptors or K\(^{+}\) channels
  – Synchronized bursts result in spike on EEG

• Seizure propagation
  – prevented by hyperpolarization and inhibitory neurons
  – Increased extracellular K\(^{+}\), accumulation of Ca\(^{2+}\) in presynaptic terminals, NMDA receptor activation → Ca\(^{2+}\) influx, change in tissue osmolarity and cell swelling
  – Propagate via local connections or long commissural pathways
Evaluation for seizure

• Most patients who have seizures do not have epilepsy
• **New onset seizures, breakthrough seizures in epilepsy, conditions mimic seizures**
• Vital signs, oxygenation, stop seizure
• History, examination, diagnostic tests, imaging
• **Therapy** – antiepileptic for structural lesion or abnormal EEG

EEG limitation and value

- The absence of electrographic seizure activity does not exclude seizure disorder (focal)
- EEG is always abnormal during generalized tonic-clonic seizures
- Interictal EEG may be normal in epilepsy, interictal epileptiform activity consists of abnormal discharges (spikes, sharp waves)
- Classification of seizure and selection of antiepileptic therapy
- Assess prognosis of seizure disorder
- Video EEG, continuous EEG
Differential diagnoses of seizures

- Syncope
- Psychogenic seizures
- Hyperventilation
- Delirium tremens
- Psychoactive drugs
- Migraine
- Movement disorders
Treatment of seizures and epilepsy

• Treatment of underlying conditions
  – Metabolic disorder, drugs, CNS lesion

• Avoidance of precipitating factors
  – Sleep deprivation, alcohol

• Suppression of recurrent seizures
  – Antiepileptic drug, preferable single medication
  – Recurrent seizures of unknown etiology or known cause that cannot be reversed
    – (1) Abnormal neurology, (2) status epilepticus, (3) post ictal Todd’s paralysis, (4) family history, (5) abnormal EEG

• Address psycho-social issues
Action of antiepileptic drugs

- Blocking **initiation** and **spread** of seizures
- Inhibition of Na\(^+\) dependent action potentials (phenytoin, carbamazepine, lamotrigine, topiramate)
- Inhibition of voltage gated Ca\(^{2+}\) channels (phenytoin, gabapentin, pregabalin)
- Attentuation of glutamate activity (lamotrigine, topiramate)
- Potentiation of GABA receptors (benzodiazepines, barbiturates)
- Increase availability of GABA (valproate, gabapentin)
- Modulate release of synaptic vesicles (levetiracetam)
First line antiepileptic drugs

- Generalized tonic clonic seizures: **Valproic acid** (bone marrow suppression, hepatotoxicity), **lamotrigine** (SJS), topiramate (psychomotor slowing, risk in glaucoma and renal stones)
- Focal seizures: **Carbamazepine** (leucopenia, hepatotoxicity, skin reaction in Asian carrying HLA 1502), lamotrigine, **phenytoin** (saturation kinetics, hirsutism, gingival hypertrophy), levetiracetam
- Typical absence (Valproic acid, ethosuximide)
- Atypical absence, myoclonic, atonic (Valproic acid, lamotrigine, topiramate)
- Dose related side effects: sedation, ataxia, diplopia
- To minimize side effects start lowest dose, increase after 5 or more half lives (c.f. the priority on stopping seizure in attack)
- Serum drug levels measure total drug (free and protein bound), increased ratio of free to bound drug in low serum proteins (sub therapeutic drug level) and free drug adequate for seizure control
Adding and stopping therapy

• The goal of monotherapy
• Refractory epilepsy: multiple drugs, surgery, vagal nerve stimulation
• Favor seizure free after discontinue therapy: (1) complete seizure control for one to five years, (2) single seizure type, (3) normal neurology, (4) normal EEG
• Reduce dose over three months
Other issues

- Psychosocial and interictal (memory, attention)
- Employment, driving and other activities
- Mortality (2 to 3 times greater, SUDEP)
- Women and epilepsy
  - Catamenial epilepsy (estrogen and progesterone)
  - Pregnancy (seizure unchanged in 50%, PK, drug)
  - Fetal abnormalities (5 to 6%, Valproic acid)
  - Contraception (decrease efficacy by CZ, PH, PB)
  - Breast feeding should be encouraged
Status epilepticus (SE)

- **Self sustaining** within 15 to 30 min (animals)
- Distinct **damages** after 30 min of seizure
- Time dependent **pharmacoresistance**
- Delay in starting treatment → Prognosis
Definitions

- **Established SE** – continuous seizure lasting 30 min or intermittent seizures lasting 30 min during which consciousness is not regained
- **Impending SE** – continuous or intermittent seizures lasting more than 5 min, without full recovery of consciousness between seizures
- **Subtle SE** – motor and EEG expression become less florid in prolonged seizures, more subtle in encephalopathy
- **Partially treated SE** – continuation of electrographic seizure activity despite cessation of clinical seizure
- **Refractory SE** – seizures lasting more than 2 hours or failure to respond to first and second line antiepileptic drugs
- **Malignant SE** – RSE recur within 5 days after tapering of anesthetic
Generalized convulsive SE (GCSE)

• Generalized seizures last more than 5 min, and when two or more seizures occur during which the patient does not return to baseline consciousness

• Subtle physical manifestations, rhythmic nystagmoid eye movement, low amplitude twitches of one or more fingers, coma

• Resolution of suspicious EEG pattern after benzodiazepine may be diagnostic (caution)
**Impending/Eary SE**
- Continuous or intermittent seizures lasting more than 5 min, without full recovery of consciousness between seizures.
- Needs early identification and initiation of treatment with high-dose anticonvulsants
- Stresses the importance of prehospital treatment in this phase.
- Pharmacosensitive phase as demonstrated in experiments.

**Established SE**
- Continuous seizure activity lasting 30 min or more, or
- Intermittent seizure activity lasting 30 min or more during which consciousness is not regained.
- SE becomes self-sustaining from this phase.
- SE induced neuronal damage becomes evident in animal studies
- Pharmacoresistance phase as demonstrated in experiments.

**Subtle SE**
- Seen after prolonged SE
- Can arise de novo also
- Motor & electrographic expression of seizure becomes less florid
- Treatment and prognosis same as established SE

**Resolved or completely treated SE**
ILAE Classification of SE

Generalized

• Convulsive
  – Tonic-clonic
  – Tonic
  – Clonic
  – Myoclonic

• Nonconvulsive
  – Absence

• Unilateral

• Non-classifiable

Focal

• Simple
  – Elementary
  – Motor
  – Sensory
  – Somatosensory
  – Dysphasic
  – Epilepsia partialis continua

• Complex
# Status Epilepticus Severity Score (STESS)

<table>
<thead>
<tr>
<th>Features</th>
<th>STESS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consciousness</td>
<td></td>
</tr>
<tr>
<td>Alert or confused</td>
<td>0</td>
</tr>
<tr>
<td>Stuporous or comatose</td>
<td>1</td>
</tr>
<tr>
<td>Worst seizure type</td>
<td></td>
</tr>
<tr>
<td>Simple partial, complex partial, idiopathic</td>
<td>0</td>
</tr>
<tr>
<td>Generalized convulsive</td>
<td>1</td>
</tr>
<tr>
<td>Nonconvulsive status epilepticus in coma</td>
<td>2</td>
</tr>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>&lt; 65 years</td>
<td>0</td>
</tr>
<tr>
<td>≥ 65 years</td>
<td>2</td>
</tr>
<tr>
<td>History</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>0</td>
</tr>
<tr>
<td>No or unknown</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>0 – 6</td>
</tr>
</tbody>
</table>
## STESS on treatment strategy

<table>
<thead>
<tr>
<th></th>
<th>Alive</th>
<th>Dead</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Score 0 – 2</strong></td>
<td>72 (97%)</td>
<td>2 (3%)</td>
<td></td>
</tr>
<tr>
<td>Coma induction –</td>
<td>61</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Coma induction +</td>
<td>11</td>
<td>0</td>
<td>1.000</td>
</tr>
<tr>
<td><strong>Score 3 - 6</strong></td>
<td>49 (61%)</td>
<td>31 (39%)</td>
<td></td>
</tr>
<tr>
<td>Coma induction –</td>
<td>34</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Coma induction +</td>
<td>15</td>
<td>13</td>
<td>0.301</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>121</td>
<td>33</td>
<td>154</td>
</tr>
</tbody>
</table>
Epidemiology of SE

• Incidence and recurrence age specific, highest in the young (less than 1 year old) and elderly
• Initial seizure focal in 2/3 of cases and major final form as generalized tonic clonic SE
• (Subtle) Continuation of electrographic seizure in up to 1/3 of cases
• Refractory in 1/3 of cases, increased hospital LOS and disability
• RSE recur within 5 days of tapering anesthetic in 1/3 of cases
Causes of SE

**Children**
- Infection and fever
- Remote symptomatic cause
- Low antiepileptic drug level
- Cerebrovascular accident
- Metabolic
- Idiopathic
- Hypoxia
- CNS infection
- Drug overdose
- Trauma
- Tumor

**Adults**
- Low antiepileptic drug level
- Remote cause (e.g. stroke)
- Cerebrovascular accident
- Metabolic (↓Na, renal, liver)
- Hypoxia
- Alcohol withdrawal
- Tumor
- Systemic infection and fever
- Trauma
- Drug overdose (e.g. cocaine)
- CNS infection
### Acute Seizures

- 37%
- 21%
- 42%

### Status Epilepticus

- 50-70%
- 8%
- 20-27%
- 3-14%

### Seizures or Status in the Critically Ill

- 89-100%
- 9-10%

### Refractory Status Epilepticus

- 65-69%
- 14-17%
- 17-22%

#### Acute Symptomatic
- TBI
- Ischemic Stroke
- Hemorrhage (SDH, ICH, or SAH)
- Venous Sinus Thrombosis
- CNS Infection (>50% are unidentified)
- CNS Tumor (Initial Presentation)
- Post-Neurosurgical
- Toxic (i.e. environmental, illicit substances, and medications)*
- Alcohol Withdrawal or Intoxication
- Eclampsia
- Metabolic (i.e. sepsis, liver failure, renal failure, hyperglycemia, low Na, PO4, glucose, Mg, Ca, or osmolality)
- Low AED Levels
- Miscellaneous (i.e. hypertensive encephalopathy or PRES, pyridoxine deficiency 2/2 pregnancy or INH, or TTP)

#### Progressive Symptomatic
- CNS Tumor (Incompletely or Unsuccessfully Treated)
- Chronic Infection (i.e. CJD, SSPE, HIV, or Neurosyphilis)
- Autoimmune Paraneoplastic (i.e. anti-NMDA, anti-VGKC, anti-GAD, and other anti-neuronal antibody syndromes)
- Autoimmune Inflammatory (i.e. Hashimoto’s, Lupus Cerebritis, Neurosarcoïdosis, MS, ADEM, or Rasmussen’s encephalitis)
- Metabolic (i.e. mitochondrial disorders, porphyria)
- Degenerative (i.e. Alzheimer Disease)

#### Remote Symptomatic
- TBI
- Ischemic Stroke
- CNS Infection
- Pre- and Perinatal Risk Factors
- Alcohol, not acutely withdrawing or intoxicated
- Benign/Static CNS Tumor
- ICH

#### Idiopathic or Epilepsy
- Cortical dysplasia
- Genetic epilepsy syndromes
Medications that lower seizure threshold

- Analgesics: meperidine, fentanyl, tramadol
- Antiarrhythmics: mexiletine, lidocaine, digoxin
- Antibiotics: β-lactams (benzylpenicillin, cefazolin, imipenem)
- Antidepressants: bupropion
- Antiepileptic drugs: phenytoin at supratherapeutic levels
- Baclofen
- Calcineurin inhibitors: cyclosporine, tacrolimus
- Alkylating agents: chlorambucin, busulfan
- Neuroleptics: clozapine, phenothiazines
- Lithium
- B-interferon, α-interferon
- Radiographic contrast agents (intrathecal and IV)
- Theophylline
- Withdrawal: opiates, alcohol, antiepileptic drugs
Investigations

- Diagnosis of SE is often clinical
- Investigations done to find etiology, define type of SE, differentiate from other conditions
- Brain imaging, lumbar puncture
- Assessment should not delay treatment
- Less than half of patients receive treatment before 30 min
Pathophysiology

• From isolated seizure to SE
  – Lower seizure threshold, failure in inhibitory mechanisms, excessive excitation (glutamate)

• Time dependent pharmacoresistance
  – Decreased potency of benzodiazepine by 20 min

• Seizure induced neuronal injury and death
  – Mitochondrial dysfunction, apoptosis, increased neuron specific enolase (neurone death marker)
Mesial temporal hyperintense signal on MRI FLAIR in GCSE
Phase 2:
(greater than 30 minutes, can be hours)

Increase in seizure minutes from minutes to hours

Airway: Decrease in sensitivity of laryngeal reflexes; high risk of aspiration

Breathing: Respiratory compromise, high risk of hypopnoea, apnoea, pulmonary edema

Circulation: risk of systemic hypotension, arrhythmia, decrease in cerebral blood flow.

Metabolic: risk of hypoglycemia, metabolic acidosis, hyperpyrexia. failure of cerebral autoregulation, decreased cerebral blood flow, an increase in intracranial pressure.
Complications of SE

• Cardiovascular
  – Arrhythmia, CHF, ↑/↓BP

• Respiratory
  – Apnea, laryngeal spasm, aspiration, APO, ARDS, PE

• CNS
  – Brain edema, hypoxia, hemorrhage

• Metabolic
  – Metabolic acidosis, ↑K, ↓Na, ↑/↓glucose

• Renal
  – Rhabdomyolysis, ARF

• Endocrine
  – ↑prolactin, cortisol, vasopressin, ↓weight

• Miscellaneous
  – Hyperthermia
  – DIC, dysautonomia, loss of intestinal motility, MODS, fractures
Management of SE

• Pre-hospital
  – Early treatment improve seizure control and outcome
  – Lorazepam has longer duration of action

• Acute setting
  – Airway, ABG, ECG, SBP >120mmHg, CPP>60mmHg
  – Hypoxia and respiratory acidosis → Intubation
  – Mannitol, glucose, thiamine
  – Correct underlying cause, prevent recurrence

• ICU
Pharmacotherapy of SE

- Rapid use of effective drugs in adequate doses
- The most effective antiepileptic is the first one given
- IV benzodiazepines enhance GABA inhibition of repetitive neuronal firing, response 79%
- 2\textsuperscript{nd} line: Phenytoin and valproic acid
- 3\textsuperscript{rd} line: Barbiturates, propofol
- Magnesium for seizures due to eclampsia (5g MgSO4 iv over 30 min follow by continuous iv 1g/hr, target serum Mg 1.7 to 3.0 mmol/L)
- Isoflurane, levetiracetam, topiramate
- Clonazepam for myoclonus following hypoxia
Treatment algorithm

**Setting**

**Seizure treatment**

**Additional measures**

**Setting**
- **Prehospital**
  - **Main sequence**
    - Lorazepam
  - **Alternatives**
    - Fosphenytoin
    - Valproic acid
    - Levetiracetam
    - Phenobarbital

**Secure airway**
- Assess ABC
- Thiamine + Dextrose
- Cardiac telemetry
- Blood work
- Brain imaging
- ± LP
- EEG if unconscious

**Setting**
- **ED**
  - Fosphenytoin
  - Levetiracetam
  - Phenobarbital

**Setting**
- **ICU**
  - Midazolam
  - Propofol
  - Pentobarbital

**Setting**
- Ketamine
- Isoflurane
- Hypothermia

**Setting**
- Intubation and MV
- Continuous EEG
- Vasopressors if needed
Treatment algorithm

Impending and early SE (5-30 min)
- Intravenous benzodiazepine
  - Lorazepam 0.1 mg/kg, or clonazepam 0.015 mg/kg, or midazolam 0.2 mg/kg

Established and early refractory SE (30 min-48 h)
- Generalised-convulsive (or subtle) SE
  - Intravenous midazolam
    - 0.2 mg/kg → 0.2-0.6 mg/kg/h and/or
    - Intravenous propofol
      - 2 mg/kg → 2-10 mg/kg/h*

Focal-complex, myoclonic, or absence SE
- Further intravenous or oral antiepileptic drug
  - Valproate*, levetiracetam, lacosamide, topiramate, pregabalin, or other

Late refractory SE (>48 h)
- Intravenous midazolam
  - 0.2 mg/kg → 0.2-0.6 mg/kg/h and/or
  - Intravenous propofol
    - 2 mg/kg → 2-10 mg/kg/h*
- Pentobarbital (thiopental)
  - 5 mg/kg (1 mg/kg) → 1-5 mg/kg/h
- Other drugs
  - Lidocaine, verapamil, magnesium, immunomodulation
- Other anaesthetics
  - Isoflurane, desflurane, ketamine
- Other approaches
  - Surgery, VNS, rTMS, ECT, hypothermia, ketogenic diet
<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism</th>
<th>Loading dose</th>
<th>Infusion rate</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lorazepam</td>
<td>GABA agonist</td>
<td>0.1mg/kg</td>
<td>2mg/min</td>
<td>Sedation, respiratory depression</td>
</tr>
<tr>
<td>Diazepam</td>
<td>GABA agonist</td>
<td>0.2mg/kg</td>
<td>5mg/min</td>
<td>Sedation, respiratory depression</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Prolong recovery of Na channels</td>
<td>20mg/kg</td>
<td>50mg/min</td>
<td>Hypotension, arrhythmia, soft tissue necrosis</td>
</tr>
<tr>
<td>Valproic acid</td>
<td>Act on Na and Ca channels, GABA receptor</td>
<td>25-45mg/kg</td>
<td>Up to 6mg/kg/min</td>
<td>Hyperammonemia, dose related thrombocytopenia, cytochrome P450 inhibitor</td>
</tr>
<tr>
<td>Levetiracetam</td>
<td>Synaptic vesicle ligand SV2A inhibits Ca channel current</td>
<td>20mg/kg</td>
<td>Over 15 min</td>
<td>Renal clearance, sedation, thrombocytopenia, LFT</td>
</tr>
<tr>
<td>Phenobarbital</td>
<td>Modulate GABA receptor</td>
<td>15-20mg/kg</td>
<td>100mg/min</td>
<td>Hypotension, respiratory depression</td>
</tr>
<tr>
<td>Midazolam</td>
<td>Modulate GABA receptor</td>
<td>0.2mg/kg</td>
<td>0.2 to 5mg/kg/hr</td>
<td>Sedation, hypotension, respiratory depression, tachyphylaxis</td>
</tr>
<tr>
<td>Propofol</td>
<td>Modulate GABA receptor, act on Na and Ca channels and NMDA receptor</td>
<td>2mg/kg</td>
<td>2-10mg/kg/hr</td>
<td>Sedation, hypotension, respiratory depression, infusion syndrome</td>
</tr>
<tr>
<td>Pentobarbital / Thiopental</td>
<td>Modulate GABA (different receptor isoform), NMDA receptor antagonist</td>
<td>5-10mg/kg</td>
<td>1-5mg/kg/hr</td>
<td>Sedation, hypotension, respiratory &amp; myocardial depression, ileus, liver dysfunction, infection</td>
</tr>
</tbody>
</table>
Refractory SE (RSE)

• Associated with acute potentially fatal causes (e.g. encephalitis, stroke)
• Electrographic seizure activity present in up to half of patients after cessation of clinical GCSE
• Treatment failure in continuous iv: Midazolam 21%, Propofol 20%, Pentobarbital 3%
• Treatment is not evidence based. Intense metabolic and electrical suppression may reduce seizure recurrence. Anesthetic therapy plus cEEG monitoring in ICU is probably the strategy
• Maintain seizure suppression for 12 to 24 hours plus adequate serum level anticonvulsants before tapering of anesthetic agent over 6 to 24 hours on cEEG monitor
## Choice of anesthetic for RSE

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism</th>
<th>Half life</th>
<th>Advantage</th>
<th>Disadvantage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midazolam</td>
<td>Modulation of GABA receptor</td>
<td>Short, 6-50 hr after prolonged administration</td>
<td>Combination with Propofol, safest profile. (↓ hypotension c.f. thiopental)</td>
<td>Tachyphylaxis</td>
</tr>
<tr>
<td>Propofol</td>
<td>Modulation of GABA receptor, Na, Ca channel, NMDA receptor</td>
<td>Short. Avoid &gt;5mg/kg/hr for over 48 hours</td>
<td>Rapid titration and withdrawal (Reduce IPPV c.f. thiopental)</td>
<td>Impairment of mitochondrial activity, use free fatty acid</td>
</tr>
<tr>
<td>Thiopental (metabolite of pentobarbital)</td>
<td>Modulation of GABA receptor, NMDA receptor antagonist</td>
<td>Long, up to 36 hr, accumulate in fat tissue</td>
<td>Complete cerebral suppression (Achieve more burst suppression c.f. Propofol)</td>
<td>Long elimination time</td>
</tr>
</tbody>
</table>
EEG target

- **Uncertainty** on targets for seizure suppression, burst suppression or flat recording
- Uncertainty on optimal length and tapering of anesthetic treatment
- For midazolam, target EEG burst suppression with inter-burst interval about 10 seconds for **24 hours**
- In critically ill comatose patients, recommend cEEG for **48 hours** to look for nonconvulsive seizure or SE
- Regard lateralized periodic discharge as ictal interictal continuum associated with nonconvulsive seizure or SE, cEEG for 48 hours and give non-sedating antiepileptic drug for period of acute illness
- Difficult to differentiate between drug induced burst suppression and seizure suppression by automated amplitude integrated measure of 2-channel EEG (bispectral index)
EEG burst suppression
### Other pharmacological approach

<table>
<thead>
<tr>
<th>Drug</th>
<th>Advantage</th>
<th>Disadvantage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoflurane</td>
<td>In part on GABA receptor, fast acting, 1.2-5%</td>
<td>Gas delivery system, possible neurotoxicity</td>
</tr>
<tr>
<td>Ketamine</td>
<td>NMDA receptor antagonist, up to 7.5mg/kg</td>
<td>Possible neurotoxicity, use with benzodiazepines</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>Act on Na channel, bolus up to 5mg/kg, iv 6mg/kg/h</td>
<td>Cardiac monitoring, possible seizure induction</td>
</tr>
<tr>
<td>Magnesium</td>
<td>↑NMDA receptor blockade, stabilize endothelium</td>
<td>Possible induction of neuromuscular blockade</td>
</tr>
<tr>
<td>Levetiracetam, Lacosamide</td>
<td>SV2A inhibit Ca channel ↑ inactivation Na channel</td>
<td>Thrombocytopenia, LFT PR interval prolongation</td>
</tr>
<tr>
<td>Ketogenic diet</td>
<td>Action through metabolic acidosis (e.g. Ketocal 4:1)</td>
<td>Refer dietitan, ketonuria and hypoglycemia</td>
</tr>
<tr>
<td>Immunological therapy (corticosteroid, PE, IVIG)</td>
<td>RSE immunological process</td>
<td>Exclude infection before treatment</td>
</tr>
</tbody>
</table>
# Non-pharmacological approach

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Advantage</th>
<th>Disadvantage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resective surgery</td>
<td>Definite seizure focal in non-eloquent brain area</td>
<td>Not for multifocal SE, surgical risk</td>
</tr>
<tr>
<td>Vagal nerve stimulation</td>
<td>Progressive titration up to 1.25mA</td>
<td>Transient bradycardia or asystole</td>
</tr>
<tr>
<td>Repetitive transcranial magnetic stimulation</td>
<td>Non-invasive, 0.5-1Hz, may apply after high frequency</td>
<td>Possible seizure induction, need repetitive treatment</td>
</tr>
<tr>
<td>Electroconvulsive therapy</td>
<td>Induce signal pathway, ↑refractory period, 1-4 daily</td>
<td>Possible seizure induction</td>
</tr>
<tr>
<td>Therapeutic hypothermia</td>
<td>Reduce epileptic discharge, 31-36°C, plus midazolam</td>
<td>Ileus, avoid barbiturates, seizure recur in rewarming</td>
</tr>
<tr>
<td>Classical music</td>
<td>Unknown mechanism</td>
<td>Reported in few patients</td>
</tr>
</tbody>
</table>
Prognosis

- **Mortality of SE**: 11% to 34%, higher in adults and often related to anoxia, stroke, metabolic abnormality, brain tumor or head injury, mortality of **refractory SE** 50% or 3 times SE

- **Outcome prediction variables** include (1) etiology, (2) time from SE onset to treatment, (3) seizure duration, (4) age, (5) response to early treatment

- Cerebral anoxia SE (burst suppression EEG) or non-reactivity during therapeutic hypothermia suggest severe brain damage and poor outcome

- **Morbidity**: SE recurrence, epilepsy (41%), seizure risk ↑3 times, cognitive impairment, return to baseline function after refractory GCSE (21%), long term care (10%)
EEG non-reactivity
EEG reactivity on stimulation (e.g. pharyngeal suction)
Reminders

• Status epilepticus is the 2\textsuperscript{nd} most frequent neurologic emergency (1st: acute stroke)
• Seizures lasting for more than a few minutes should be treated immediately, especially GCSE
• More conservative approach for nonconvulsive SE with preserved consciousness
• Negative predictive value of STESS on treatment strategy based on age, seizure type, consciousness impairment, previous seizure
• Avoid complications of over treatment in mimics, e.g. movement disorders, clonus in spasticity, shivering, psychogenic (serum lactate, prolactin, CK)
• Patients with RSE may recover with good functional outcome, continue supportive treatment if neuroimaging is relatively normal in young patients, even if prolonged intensive care is required
A 22 years old woman was admitted into medical ward for dizziness and headache. She has enjoyed good past health and work as a clerk. There was no recent travel or contact history. After admission she was noted to be confused and displayed limb twitching. Two doses of diazepam 5mg IV and one dose of phenytoin 1000mg IV have been given. Limb twitching has decreased but the patient remained unconscious. ICU was consulted.

(1) What was the patient suffering from? (2) What are the possible common causes in this patient? (3) How will you manage this patient? (4) What is drug treatment strategy? (5) What are the possible complications that will occur in this patient? (6) All initial work up were negative, what diagnosis should be excluded in this patient and how?
References

• Seizure and epilepsy. DH Lowenstein. Harrison’s Principles of Internal Medicine 2012, 3251-3259
• Seizures and status epilepticus. S Pati and JJ Sirven. Emergency Neurology (KL Roos, Editor) 2012, 179-194
• Prognostic value of continuous EEG monitoring during therapeutic hypothermia after cardiac arrest. AO Rossetti et al. Critical Care 2010 (14): R173