



โครงการ ศูนย์ความเป็นเลิศโรคลมชักรามาธิบดี
(Rama Epilepsy Excellent Center)

Difficult issues in managing seizures in the critically ill patients

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Seizures in the critically ill patients

- A manifestation of either a primary central nervous system (CNS) insult or a systemic disorder with secondary CNS effects.
- Most organs can be secondarily affected by the ongoing seizure activity or as a consequence of treatment.

Management of seizures in critically ill patients

- Principle of treatment

1. achieves seizure control

- rapid treatment of clinical and electrographic seizures

2. identifies and treats the underlying cause

3. prevents, identifies, and manages systemic complications

Difficult issues in managing seizures in the critically ill patients

1. Diagnosis of seizure
2. Management of seizure
3. Management of complication
4. Monitoring clinical response

1. Diagnosis of seizure

- Difficult issues
 - Detection and diagnosis may be difficult due to the various comorbidities seen in intensive care unit (ICU) patients.
 - Early diagnosis and treatment is very important in improving the clinical outcomes.

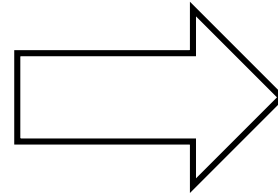
Clinical clues for diagnosis of epileptic events in the intensive care units (ICU)

- History taking from a witness

- Neurologic examination

- level of consciousness

- clinical signs



seizure

OR

not a seizure?

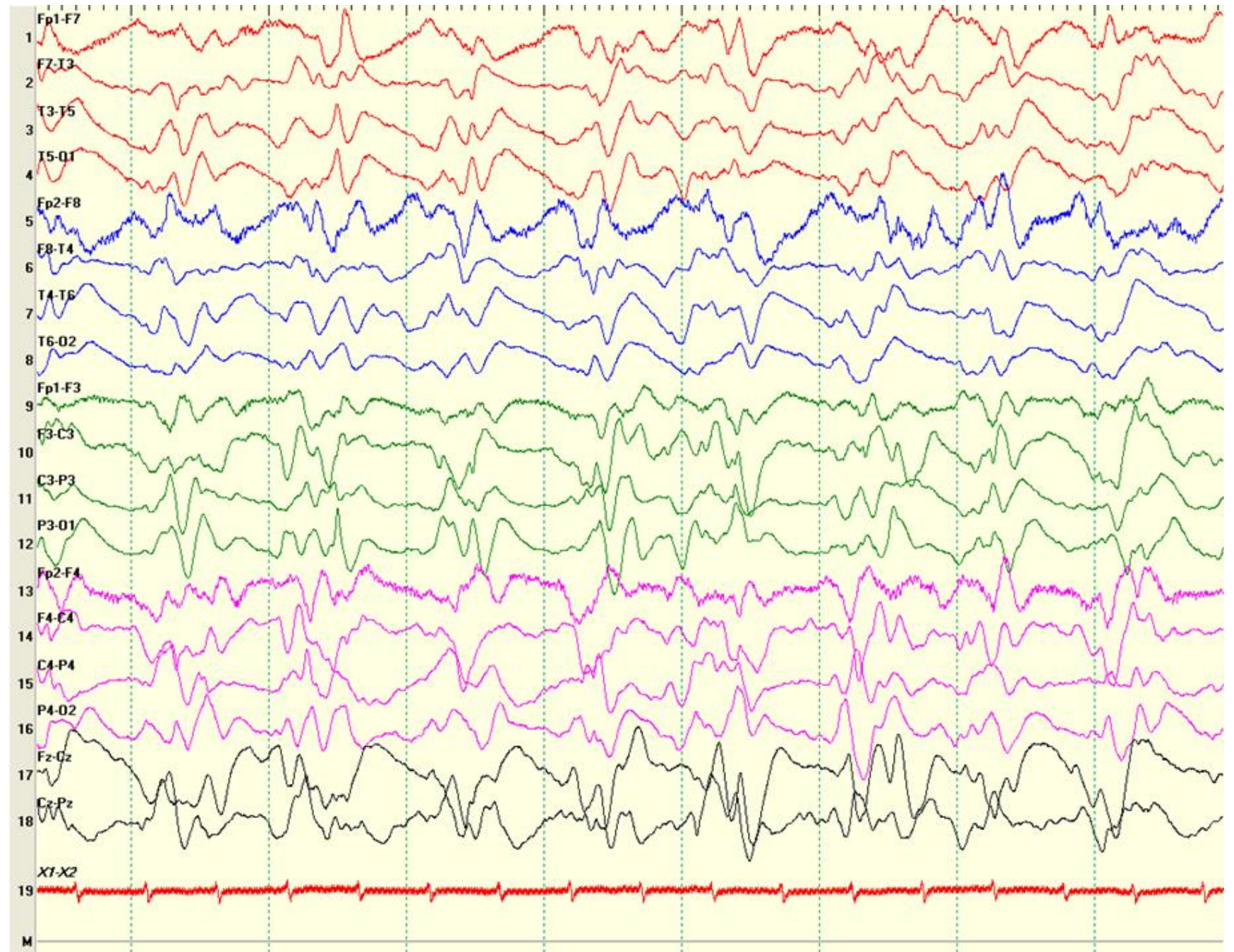
Indication for electroencephalography(EEG)

- Diagnosis of epileptic event
 - alteration of consciousness
- Diagnosis of non- epileptic events and/or recurrent spells
 - abnormal movements
- Therapeutic monitoring

Cases #1

- A 71-yo presents with ruptured left supraclinoid internal carotid artery aneurysm s/p coiled embolization and altered mental status. Neuroimaging showed subarachnoid hemorrhage. After the operation, The patient had been confused off and on for an hour.
- History of phenytoin-induced rash
- Routine EEG: Non-convulsive status
- Treatment: levetiracetam 500mg IV q 12 hours

Cases #1



Diagnosis:
Non-convulsive status epilepticus

2. Management of seizure

- Difficult issues
 - refractory status epilepticus (RSE)
 - choosing the anti-seizure medication
 - worsening medical conditions
 - drug interactions

Choosing the anti-seizure medications

- Age
- Clinical seizure type
- Comorbidities
 - cardiovascular disease
 - liver disease
 - kidney disease
- History of drug allergy
 - minor rash to SJSs
- Anti-seizure medications
 - administration
 - mechanism of action
 - pharmacodynamics
 - pharmacokinetics
 - efficacy for each seizure type
 - recommended doses
 - adverse effects
 - drug interactions

Status epilepticus

- First-line agents
 - diazepam IV/ rectal
 - midazolam IV or IM or intrabuccal or intranasal
 - lorazepam IV
- Second-line agents
 - phenytoin IV
 - phenobarbital IV
 - sodium valproate IV
 - levetiracetam IV

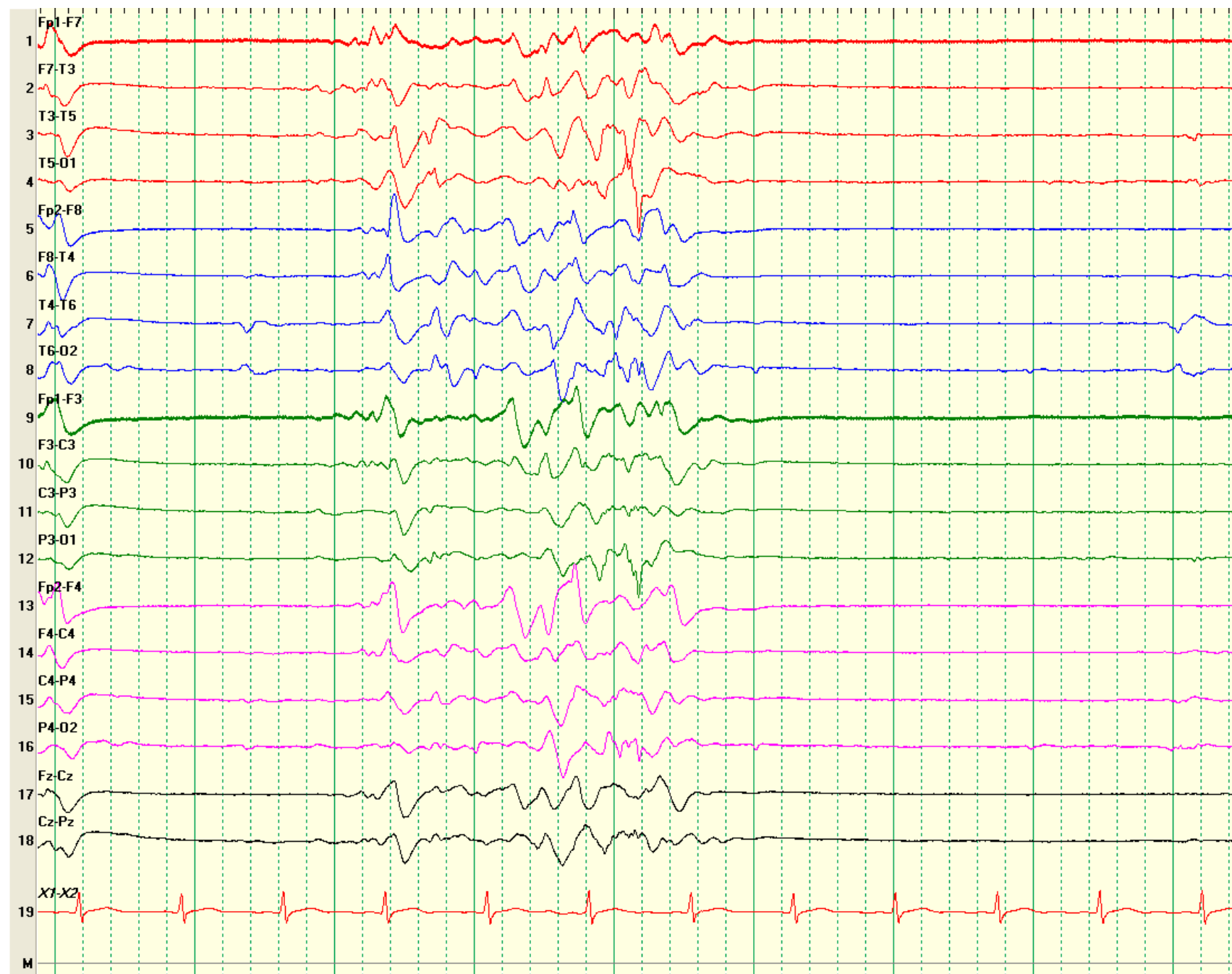


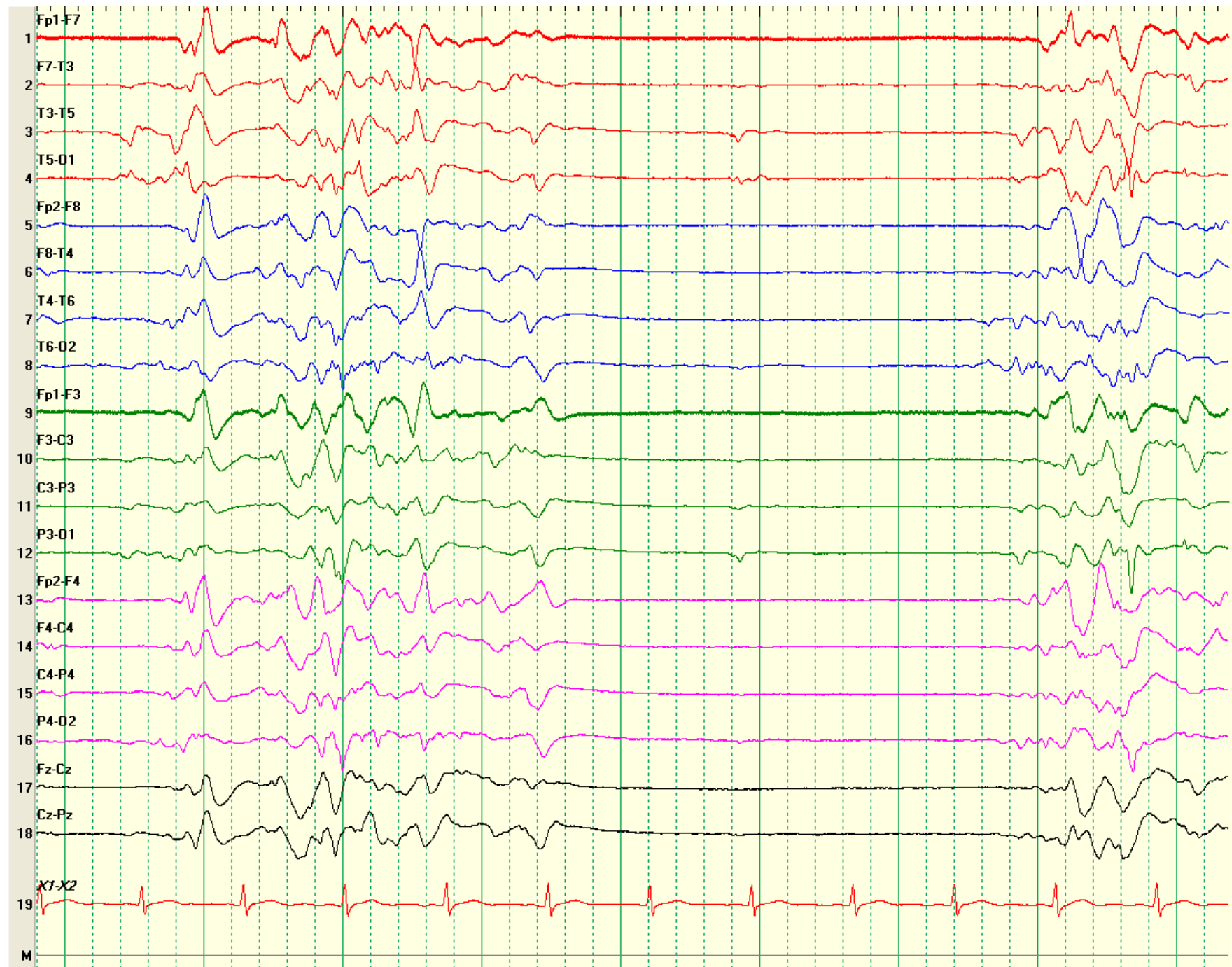
Thailand clinical practice guidelines for epilepsy

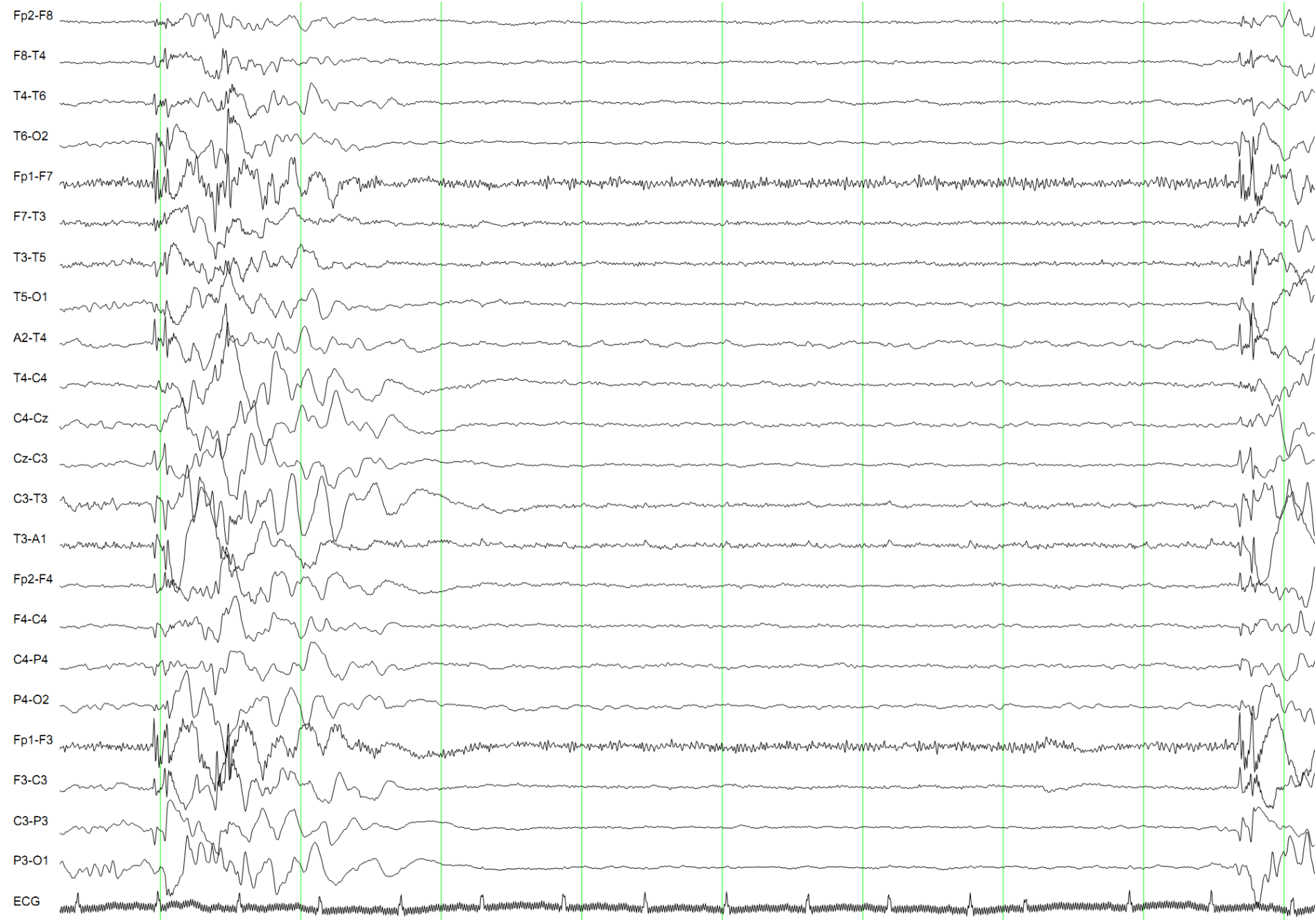
<http://thaiepilepsysociety.com/>

Anesthetic agents for the treatment of refractory status epilepticus (RSE)

- Controversy
 - 1. stop the electrographic seizure
 - 2. burst suppression
 - 3. complete background suppression
- Achieves seizure control for 24 to 48 hours







Fp1-F7
50 μ V

F7-T7

T7-P7

P7-O1

Fp2-F8

F8-T8

T8-P8

P8-O2

Fp1-F3

F3-C3

C3-P3

P3-O1

Fp2-F4

F4-C4

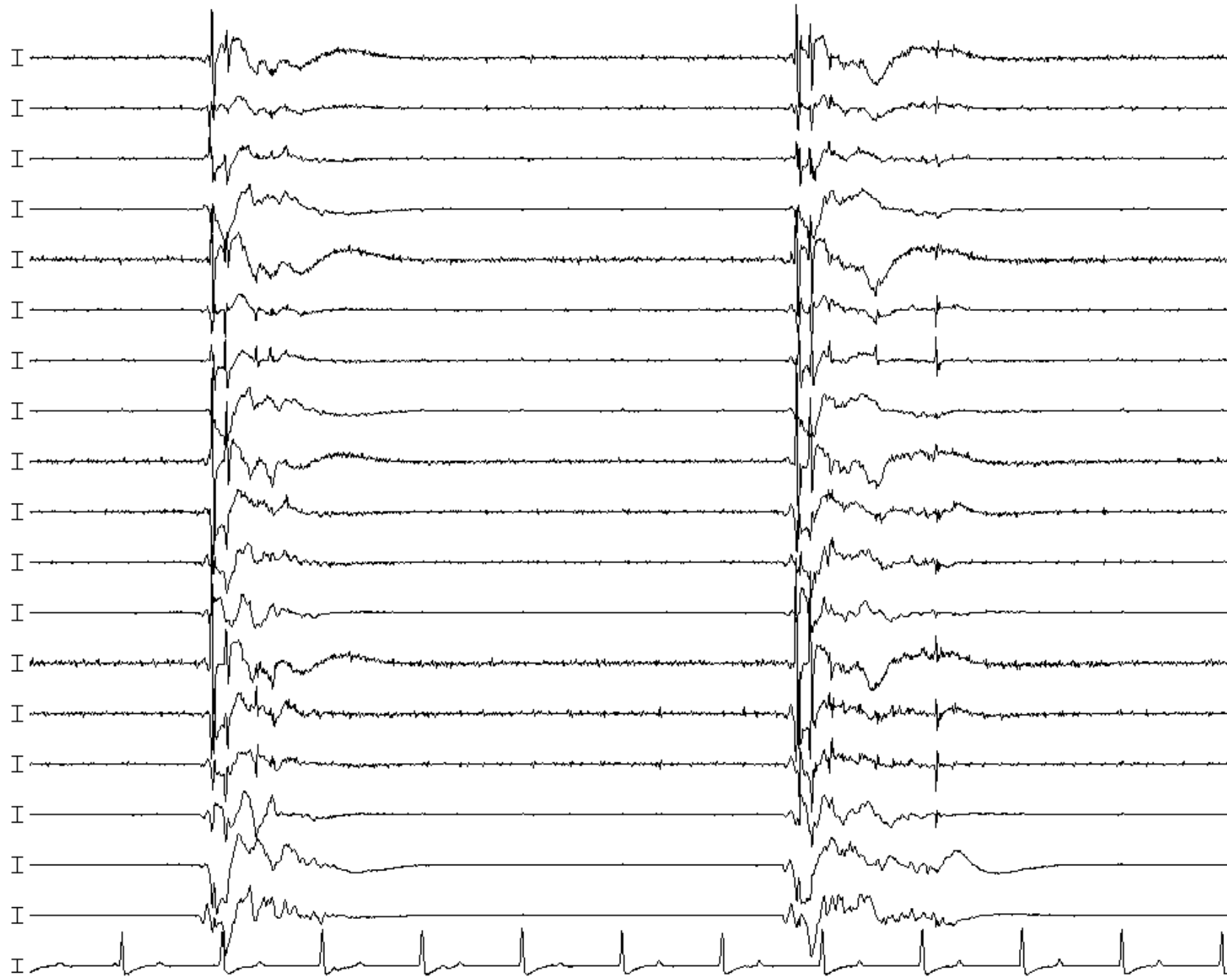
C4-P4

P4-O2

Fz-Cz

Cz-Pz

EKG1-EKG2
50 μ V



Anesthetic agents in refractory status epilepticus

	Loading dose	Initial rate	Maintenance dose	Side effects
Midazolam	0.2 mg/kg IV over 2 to 5 minutes; repeat 0.2 to 0.4 mg/kg boluses every 5 minutes until seizures stop, up to a maximum loading dose of 2 mg/kg	0.1mg/kg/hr	0.05 to 2.9 mg/kg/hr	Hypotension, respiratory depression
Propofol	1 to 2 mg/kg IV over 3 to 5 minutes; repeat boluses every 3 to 5 minutes until seizures stop, up to maximum total loading dose of 10mg/kg	20 microgram/kg/min; bolus and increase rate until seizure control	30 to 200 microgram/kg/min titrated to EEG with 5 to 10 microgram/kg/min every 5 minutes or 1 mg/kg bolus for breakthrough status epilepticus	Respiratory suppression, hypotension, propofol infusion syndrome(PRIS)
Pentobarbital	5 to 15 mg/kg infused over 1 hour; may repeat 5 mg/kg boluses until seizures stop	1 mg/kg/hr	0.5 to 5 mg/kg/hr, titrated to maintain seizure suppression pattern on EEG and a serum level of 30-45 microgram/ml; for breakthrough status epilepticus, a 5 mg/kg must be given, and the continuous infusion rate should be increased by 0.5-1 mg/kg/hr every 12 hours	Hypotension, respiratory depression, allergic reactions, immunosuppression
Ketamine	1 to 4.5 mg/kg with supplements of 0.5-2.5 mg/kg every 30-45 minutes or 10 to 50 microgram/kg/min	1.5 mg/kg every 3 to 5 minutes until seizures stops, up to a maximum of 4.5 mg/kg	5 to 125 microgram/kg/min (0.3-7.5 mg/kg/hr)	Elevation of blood pressure, increased intracranial pressure

3. Management of complication

- Complications of status epilepticus
 - rhabdomyolysis
 - hyperthermia
 - cerebral edema secondary to status epilepticus
- Complications of treatment
 - adverse effects from medications

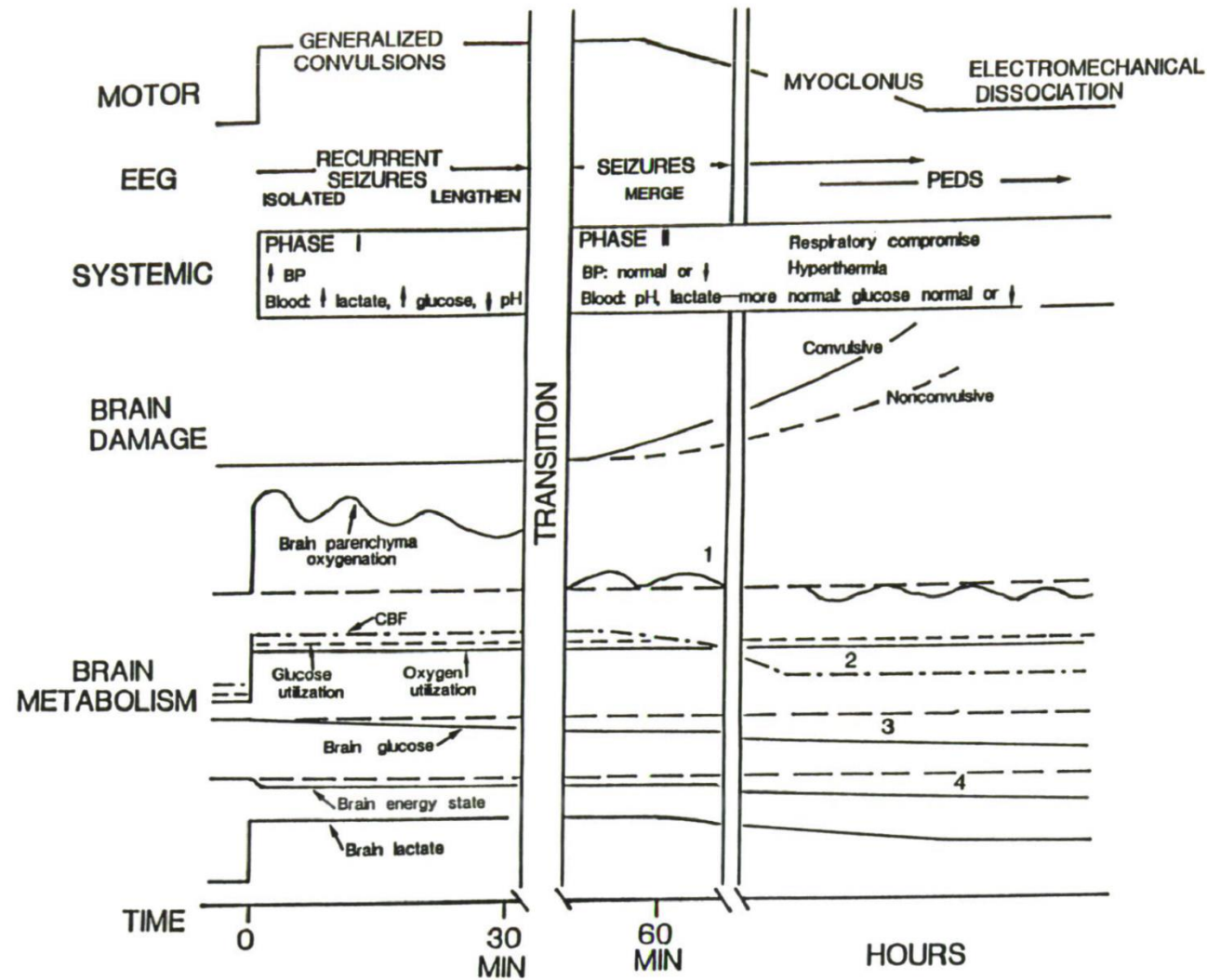


FIG. 1. Time course of pathophysiologic alterations during status epilepticus (SE). Concomitant motor and EEG manifestations are illustrated in top two lines, and specific systemic and cerebral physiologic manifestations are illustrated below. Note discontinuity in time line and designation of a critical transition period after 30 min of SE. After the transition period, brain glucose and oxygen use continue elevated, whereas cerebral blood flow and brain energy state eventually decline. (From Lothman, 1990. Reprinted with permission.)

Physiological changes in status epilepticus

Phase 1: compensation

Cerebral changes	Systemic and metabolic changes	Autonomic and cardiovascular changes
increased cerebral blood flow	hyperglycemia	increased blood pressure
increased cerebral metabolism	lactic acidosis	increased cardiac output
increased lactate concentration		massive catecholamine release
increased glucose concentration		cardiac dysthymia
		urine incontinence

Physiological changes in status epilepticus

Phase 2: decompensation

Cerebral changes	Systemic and metabolic changes	Autonomic and cardiovascular changes
failure of cerebral autoregulation	hypoglycemia	hypoxia
hypoxia	hypokalemia/ hyperkalemia	falling blood pressure
hypoglycemia	metabolic and respiratory acidosis	falling cardiac output
increased intracranial pressure and cerebral oedema	hepatic and renal dysfunction	cardiac failure
	consumptive coagulopathy	respiratory failure
	DIC	hyperpyrexia
	rhabdomyolysis, myoglobinuria	

4. Monitoring clinical response

- Difficult issues
 - how to monitor the clinical response?
 - no clinical/ subclinical seizures
 - no electrographic seizures
 - EEG interpretation?
 - correlates with clinical findings

ICU monitoring

- Hemodynamic and respiratory monitoring
 - Pulse oximetry
 - Blood pressure and heart rate monitoring
 - EKG monitoring
- Continuous EEG monitoring
 - to monitor the therapeutic response
 - to avoid side effects of treatment

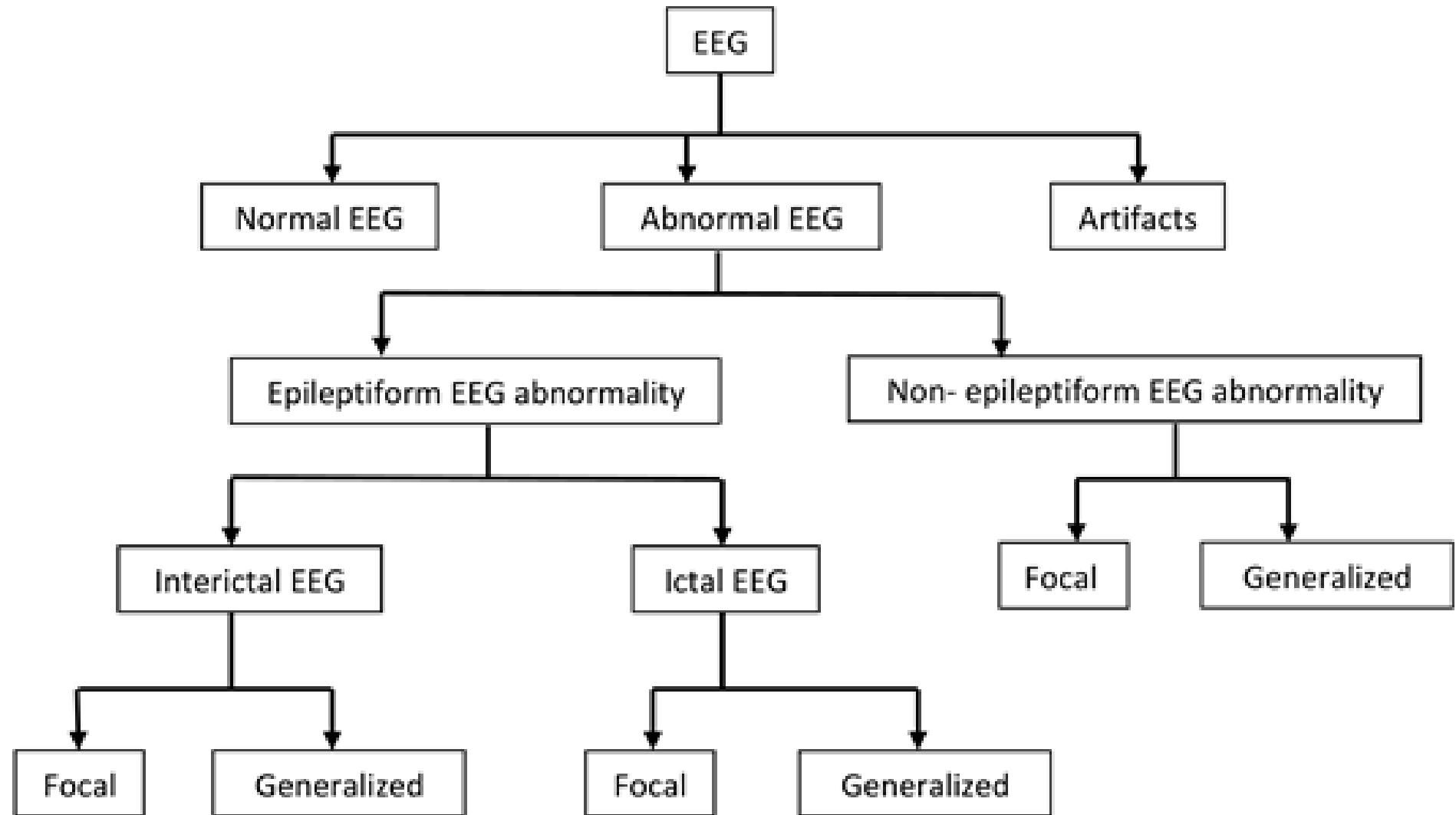


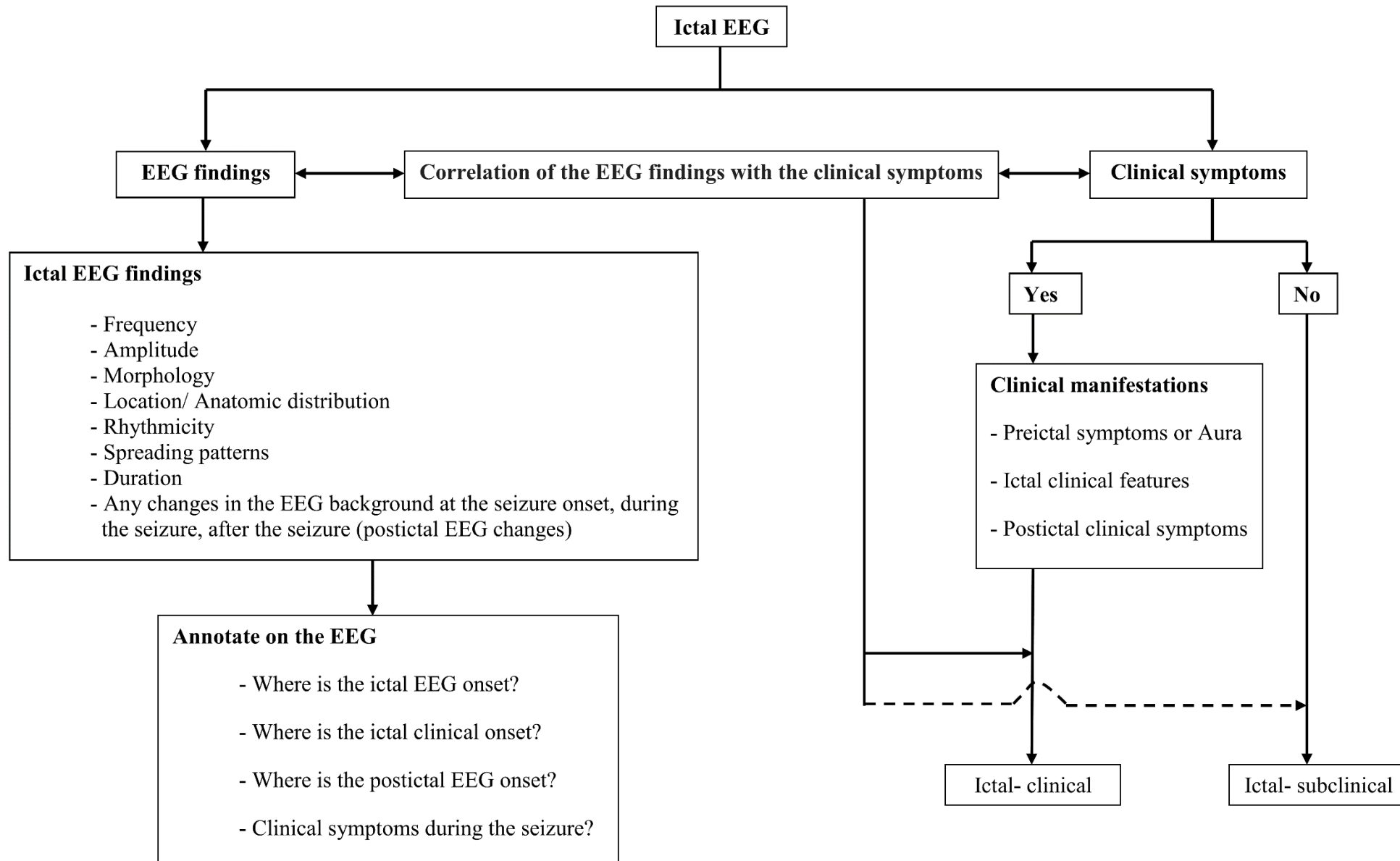
Therapeutic EEG monitoring

- Anesthetic agents should be titrated to burst suppression or isoelectric EEG
- Duration of treatment should be at least 24- 48 hours before weaning anesthetic agents and maintenance medications should be given to the patients.

EEG interpretation

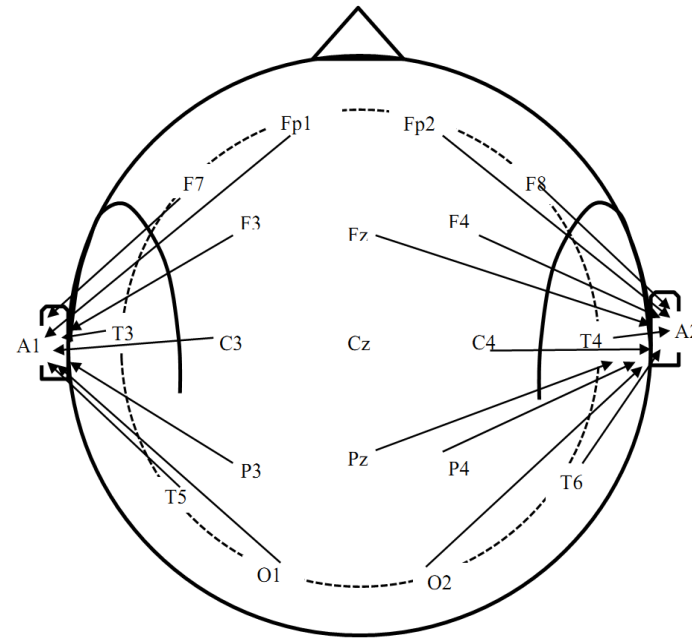
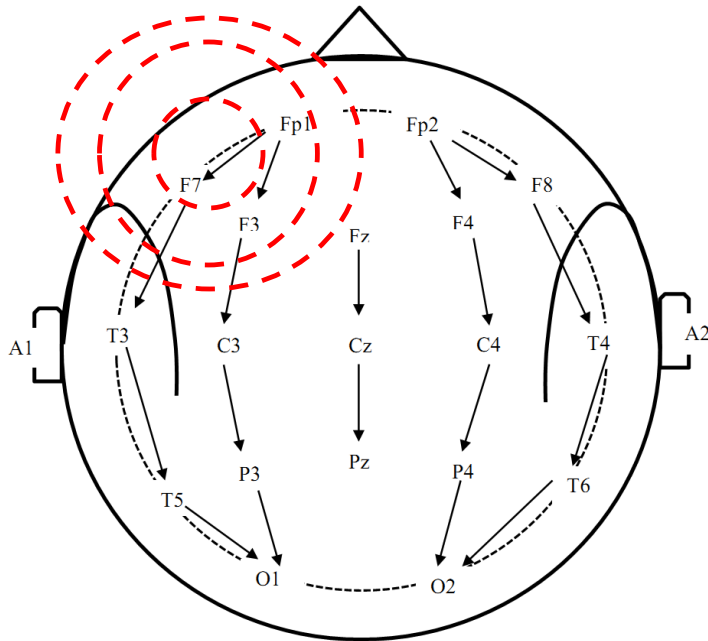
- Questions to ask yourself
 1. clinical response
 - any clinical/ subclinical seizures
 2. ICU EEG monitoring
 - EEG seizure **OR** no EEG seizure **OR** artifacts
 - controversial EEG patterns
 - neurological prognosis





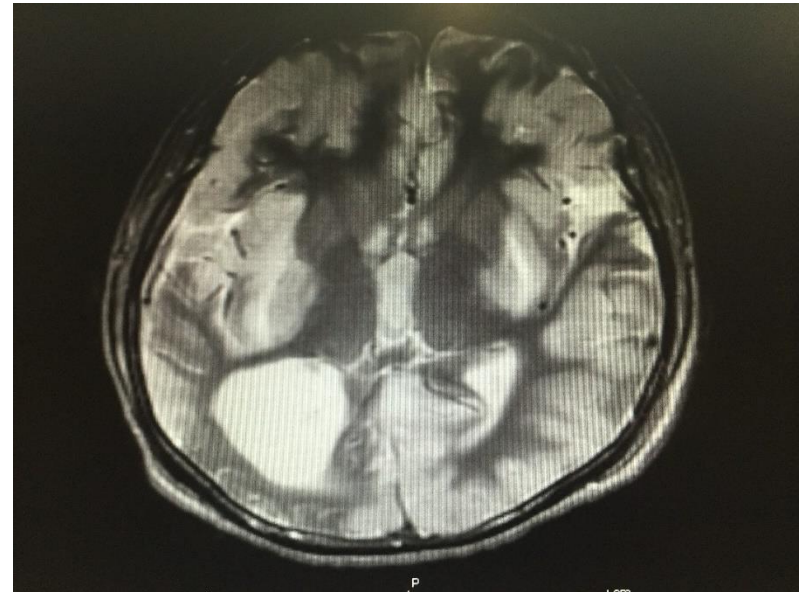
Localization of voltages in EEG

- bipolar montage vs referential montage
- electrical field
- localization of voltages in EEG

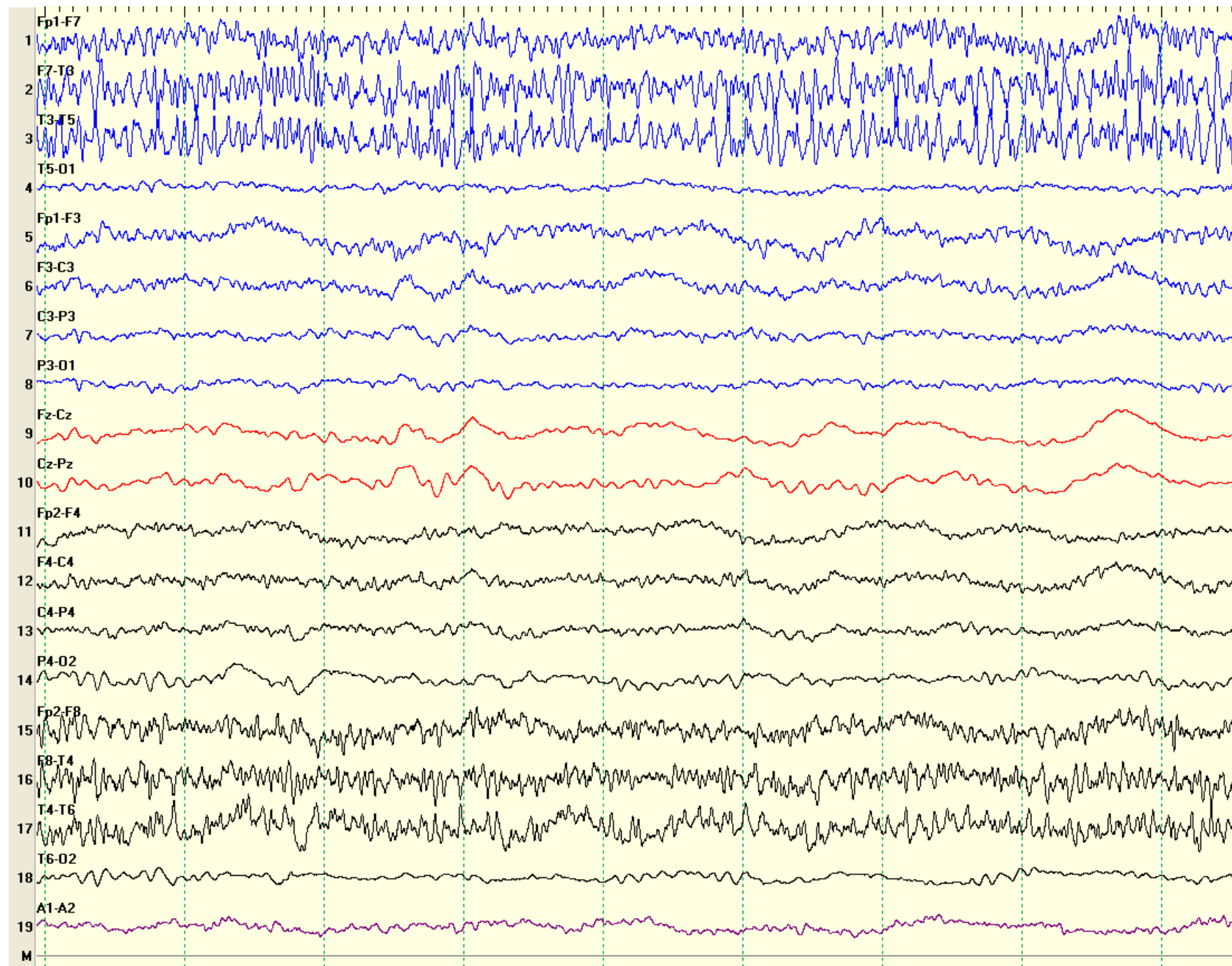


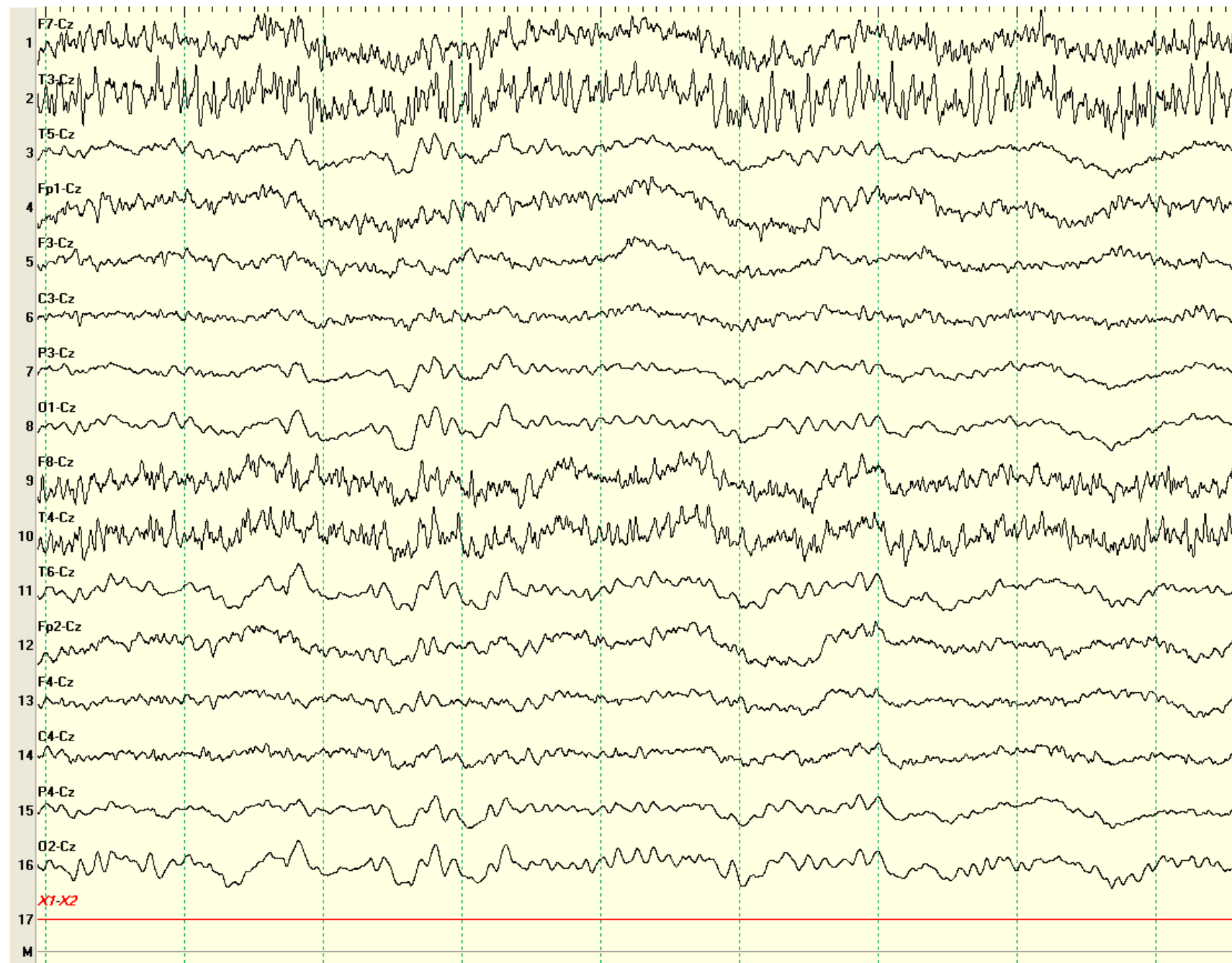
Case MELAS

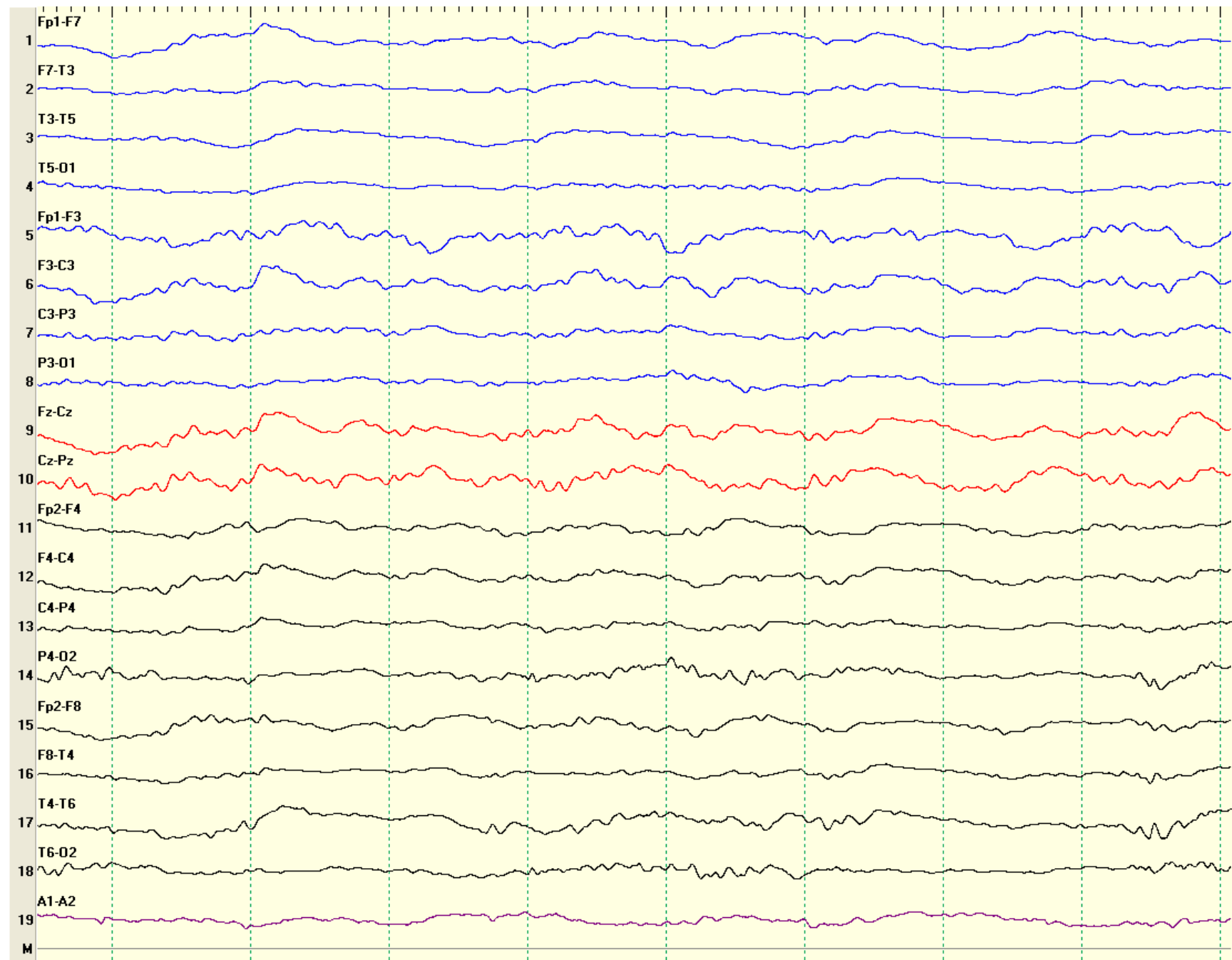
- A 17-yo male with past medical history of Mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke (MELAS) syndrome presents to the emergency department with status epilepticus for 30 minutes.



MELAS







midazolam + levetiracetam

Thank you