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Supplementary File

SEMEIOLOGY	• **With prominent motor symptoms:** ° Convulsive SE (generalised convulsive, focal onset evolving into bilateral convulsive SE, unknown whether focal or generalized) ° Myoclonic SE (with coma or without coma) ° Focal motor (repeated focal motor seizures, epilepsia partialis continua, adversive status, ictal paresis) ° Tonic status ° Hyperkinetic SE • **Without prominent motor symptoms (non-convulsive SE, NCSE)** ° NCSE with coma ° NCSE without coma ° Generalized (typical absence status, atypical absence status,myoclonic absence status) ° Focal (without impairment of consciousness, aphasic staus, with impaired consciousness) ° With impaired consciousness ° Unknown whether focal or generalized ° Autonomic SE
ETIOLOGY	• **Known (symptomatic)** ° Acute (stroke, toxic factors, encephalitis, etc.) ° Remote (infections, trauma, stroke, etc.) ° Progressive (brain tumors, neurodegenerative disorders, etc.) ° SE in defined electroclinical syndromes • **Unknown (cryptogenic)**
(interval between the onset of SE and the first EEG without epileptic activity and clinical manifestations)	**Initial** (duration <20-30 min) **Defined** (duration 30-60 min) **Refractory** (60-120 min) **Super refractory** (>24h)
EEG CORRELATES	• **Location** ° Generalized ° Lateralized ° Bilateral independent ° Multifocal • **Name of the pattern** ° Periodic discharges ° rhythmic delta activity ° spike-and-wape/sharp-and-wave plus subtypes • **Morphology** ° Sharpness ° Number of phases ° Absolute and relative amplitude ° Polarity • **Time-related features** ° Prevalence ° Frequency ° Duration ° Daily pattern duration and index ° Onset ° Dynamics • **Modulation** • **Effect of intervention on EEG**
	Neonatal (0 to 30 days) and infancy (1 month to 2 years) ° Tonic status (Ohtahara syndrome or West syndrome) ° Myoclonic status in Dravet syndrome ° Focal status ° Febrile SE • **Childhood (>2 to 12 years)** ° Autonomic SE in early-onset benign childhood occipital epilepsy (Panayiotopoulos syndrome) ° NCSE in specific childhood epilepsy sindromes and etiologies (ring chromosome 20 and other karyotype abnormalities e.g. Angelman syndrome, epilepsy with myoclonic-atonic seizures, etc) ° Tonic status in Lennox-Gastaut syndrome ° Myoclonic status in progressive myoclonus epilepsies ° Electrical status epilepticus in slow wave sleep (ESES) ° Aphasic status epilepticus in Landau-Kleffner syndrome • **Adolescence and adulthood (>12 to 59 years)** ° Myoclonic status in juvenile myoclonic epilepsy ° Absence status in juvenile absence epilepsy ° Myoclonic status in Down syndrome • **Elderly (>60 years)** ° Myoclonic status in Alzheimer's disease ° NCSE in Creutzfeldt-Jakob disease ° De novo (or relapsing) absence of later life

Table 1: Classification of Status Epilepticus according to clinical and etiological criteria.

Table 2: Principal causes of Status Epilepticus.

• **Cerebrovascular diseases** (e.g. ischemic stroke, intracerebral bleeding, subarachnoid bleeding, subdural hematoma, epidural hematoma)
• **CNS infections** (e.g. bacterial meningitis, viral encephalitis, cerebral toxoplasmosis, tuberculosis, cerebral malaria,)
• **Neurodegenerative diseases** (e.g. Alzheimer's disease, frontotemporal dementia)
• **Intracranial tumors** (e.g. glial tumors, meningioma, metastases, Lymphoma, meningeosis neoplastica)
• **Cortical dysplasias** (e. g. tuberous sclerosis complex, nodular heterotopias, lissencephaly)
• **Head trauma**
• **Alcohol related** (e.g. intoxication, Wernicke encephalopathy)
• **Intoxication** (e.g. drugs, neurotoxins)
• **Withdrawal of or low levels of antiepileptic drugs**
• **Cerebral hypoxia or anoxia**
• **Metabolic disturbances** (e.g. organ failure, acidosis, hepatic encephalopathy, radiation encephalopathy)
• **Autoimmune disorders causing SE** (e.g. multiple sclerosis, paraneoplastic encephalitis, Hashimoto's encephalopathy, Rasmussen encephalitis, Goodpasture syndrome, cerebral lupus)
• **Mitochondrial diseases causing SE** (e.g. MELAS, MERRF, Leigh syndrome)
• **Chromosomal aberrations and genetic anomalies** (e.g. Angelman syndrome, Wolf-Hirshhorn syndrome, Fragile X syndrome, X-linked mental retardation syndrome)
• **Neurocutaneous syndromes** (e.g. Sturge-Weber syndrome)
• **Metabolic disorders** (e.g. Wilson disease, Adrenoleukodystrophy, Morbus of Gaucher, Porphyria)
• **Others**

• STAGE I: Early Phase • (duration from 5 to 10 minutes)	If the intravenous (IV) route is available: • **Lorazepam** ° Dosage (IV): 0.1 mg/kg (maximum dose 10 mg) over 30-60 sec; if seizure continues in 5 min, give an additional 0.1 mg/kg. • **Diazepam:** ° Dosage (IV): 0.5 mg/kg (maximum dose 10 mg) IV bolus (maximum rate 5 mg/min); if necessary can be repeated once up to 20 mg. • **Clonazepam:** ° Dosage (IV): 1 mg IV bolus (maximum rate 0.5 mg/min); if necessary can be repeated once after 5 min. If IV route is difficult or not possible: • **Midazolam:** ° Dosage (buccal): 0.15-0.5 mg/kg (maximum dose 10 mg). ° Dosage (IM): 0.2 mg/kg (maximum dose 5 mg). • **Diazepam** ° Dosage (rectal): 0.5 mg/kg (2-5 yr); 0.3 mg/kg (6-11 yr); 0.2 mg/kg (≥12 yr.
• STAGE II: Established Status Epilepticus • (duration from 10 to 30 minutes)	• **Phenytoin/Fosphenytoin:** ° Dosage phenytoin (IV): 18-20 mg/kg over 20 min (<1 mg/kg/min; maximum, 50 mg/min); may give an additional 5 mg/kg as needed. ° Dosage fosphenytoin (IV or IM): 18-20 mg phenytoin equivalents/kg (< 3mg phenytoin equivalents/kg/min; max. < 100-150 mg phenytoin equivalents/min). • **Phenobarbital:** ° Dosage (IV): 15-20 mg/kg (maximum dose 1 g) IV bolus infusion at a max. rate of 1 mg/kg/min. • **Valproic Acid:** ° Dosage (IV): 25-30 mg/kg over 5-15 min (<3 mg/kg/min up to 200 mg/min) followed by an infusion of 1-6 mg/kg/hr. • **Levetiracetam:** ° Dosage (IV): 40-60 mg/kg, max. 3 g (administer 2-5 mg/kg/min).
	• **Lacosamide** ° Dosage (IV): 50-400 mg; 200 mg given over 15 min. • **Propofol:** ° Dosage (IV): 2 mg/kg IV bolus infusion, repeated if necessary, and then followed by a continuous infusion of 5–10 mg/kg/h initially, reducing to a dose sufficient to maintain a burst-suppression pattern on the EEG (usually 1–3 mg/kg/h). • **Thiopental** ° Dosage (IV): 100–250 mg IV bolus infusion giver over 20 s with further 50-mg boluses every 2–3 min until seizure control, followed by a continuous IV infusion at a dose sufficient to maintain a burst-suppression pattern on the EEG (usually 3–5 mg/kg/h). • **Pentobarbital** ° Dosage (IV): 5–15 mg/kg IV bolus, followed by a continuous IV infusion at a dose sufficient to maintain a burst-suppression pattern on the EEG (usually 0.5–3 mg/kg/h).
• STAGE IV: Super Refractory Status Epilepticus • (Duration > 24 hours)	The first-line therapy includes maintaining the use of anesthetic drugs used in Phase III, ad in addition to which may be used: • **Ketamine***1–3 mg/kg IV bolus, followed by a continuous IV infusion at a dose sufficient to maintain a burst-suppression pattern on the EEG (usually up to 5 mg/kg/h). • **Topiramate (Enteral)**: The dose of topiramate used in studies ranged between 2 and 25 mg/kg/day in children and up to 1600 mg/day in adults. Metabolic acidosis was the most frequently reported side effect with its use. • **Perampanel:** The initial dose in studies case of refractory & super-refractory status epilepticus is of 4 mg, titrated up to a maximum dose of 12 mg in steps of 2 to 4 mg per day. Data on PER in SE remain anecdotal and are limited to a few cases. Perampanel was used in refractory and super-refractory cases only, and this may explain the low rate of respondents in both studies. (Adam Strzelczyk, Laurent M Willems, Sophia Willig, Felix Rosenow & Sebastian Bauer (2015) Perampanel in the treatment of focal and idiopathic generalized epilepsies and of status epilepticus, Expert Review of Clinical Pharmacology, 8:6, 733-740) As second-line therapy consider: • **Hypothermia*** levels of hypothermia uncertain, usually target temperatures between 32 and 35 °C continued in the first instance for 24–48 h; • **Magnesium infusion***dose of 2–6 g/h to obtain a serum level of 3.5 mmol/L; • **Pyridoxine infusion*** (in young children): 180–300 mg; • **Immunologic therapy*** high-dose steroids (1 g/day in adults) over 3 days and continued at lower doses (1 mg/kg/day) over 1 week; in addition, course of IV immunoglobulin (0.4 g/kg/day) over 5 days or plasma exchange; other like immunomodulatory agents (such as cyclophosphamide or rituximab) or plasma exchange is rarely used, it has been tried. • **Ketogenic diet*** • **Emergency neurosurgery*** (including focal resection, multiple subpial transection, corpus callosotomy, and hemispherectomy, even in combination). As third-line therapy consider: • **Electroconvulsive therapy*;** • **Cerebrospinal fluid drainage*.** *No randomized, controlled trials available in the literature to inform about the use of this drug/procedure in this stage of status epilepticus.

Table 3: Treatment strategies of Status Epilepticus.