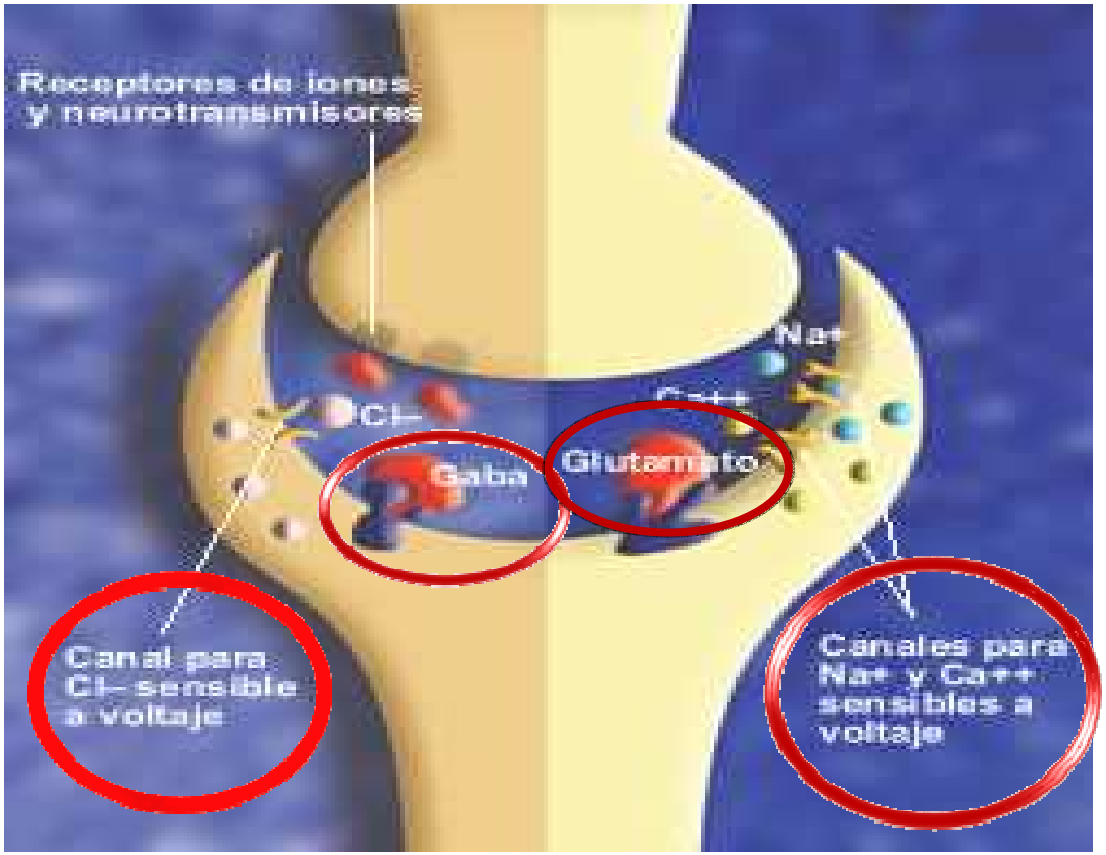
STATUS EPILEPTICO.

Dr.Nestor Wainsztein.

FCCP .FCCM .FAHA

Convulsión

Convulsión: **Cuadro clínico paroxístico de disfunción neurológica, debido a descargas anormales, excesivas, hipersincrónicas de una población neuronal.**
Cambios en el control motor, en el comportamiento o en la función autonómica.



Glia: **modula la excitabilidad neural, por medio del mantenimiento del pH extracelular y el transporte de glutamato al extracelular**

La perdida en la densidad de los receptores gabaergicos **es la causa probable del incremento de la inefectividad de las benzodiazepinas y barbituratos en controlar las convulsiones haciendo que el Status Epilepticus sea mas prolongado.**

Macdonald and Kapur, 1999).

Fisiopatología de la refractariedad

La refractariedad a los tratamientos habituales se debe a alteraciones de los receptores Gabaergicos en el hipocampo

La perpetuidad en el tiempo obedece a la estimulación sostenida de los receptores para NMDA

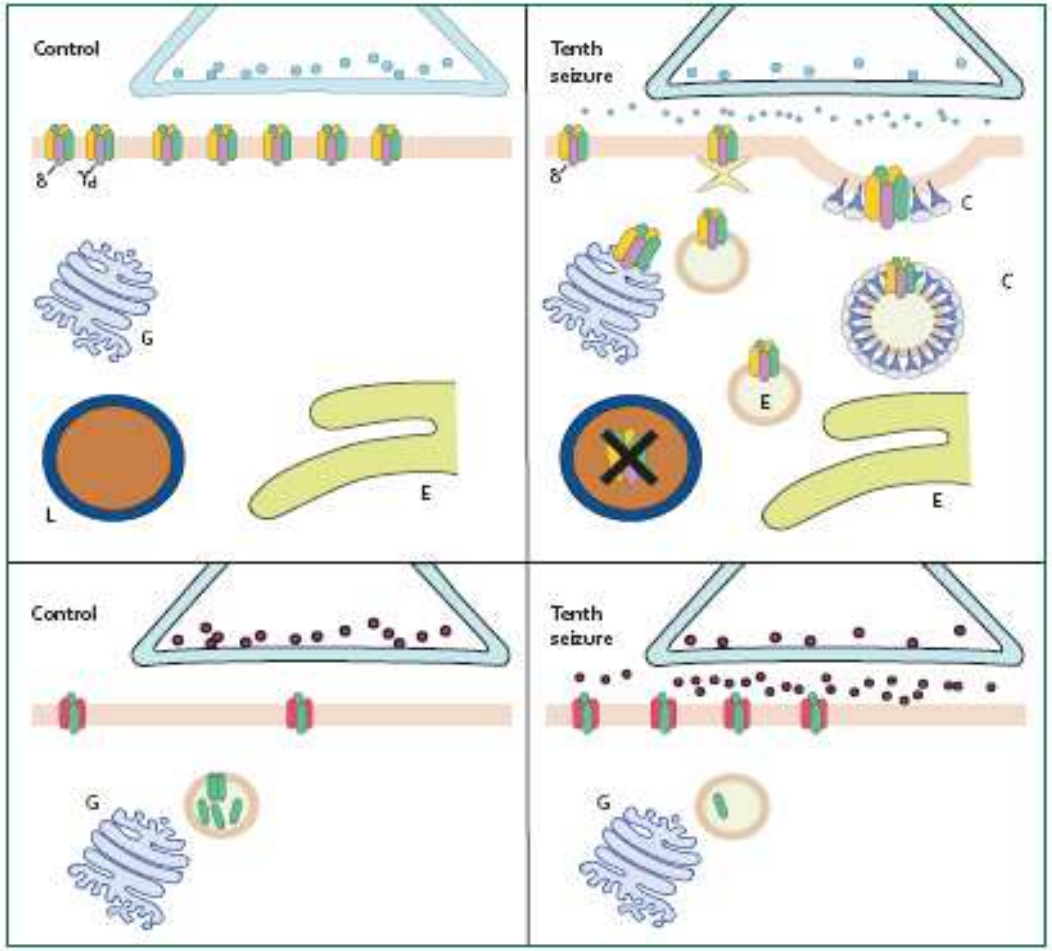


Figure 1: Model of our hypothesis of receptor trafficking in transition of single seizures to status epilepticus
Top: after repeated seizures, the synaptic membrane of $GABA_A$ receptors forms clathrin-coated pits, which internalise as clathrin-coated vesicles (C), inactivating the receptors because they are no longer within reach of the neurotransmitter. These vesicles develop into endosomes (E), which can deliver the receptors to lysosomes (L) where they are destroyed, or to the Golgi apparatus (G) from where they are recycled to the membrane. Bottom: by contrast, in NMDA synapses, subunits are mobilised to the synaptic membrane and assemble into additional receptors. As a result of this trafficking, the number of functional NMDA receptors per synapse increases whereas the number of functional $GABA_A$ receptors decreases.[11]

Lancet Neurology, marzo 2006.vol 5

Arancibia and Kittler, 2009; Smith and Kittler, 2010

Epilepsia, **48**(Suppl. 8):11–13, 2007
doi: 10.1111/j.1528-1167.2007.01336.x

MOLECULAR NATURE OF STATUS EPILEPTICUS

Changes in $GABA_A$ receptors in status epilepticus

Guenther Sperk

Table 1. Changes in the expression of $GABA_A$ receptor subunits in animal models of status epilepticus

	Kainic acid-induced status epilepticus			Electrically induced status epilepticus		
12 h	7–20 d	20 d	24 h	7–20 d	

As GABA is the principle inhibitory transmitter, this reduction in GABAergic activity may be an important reason for seizures to become persistent.

++, >150%; +, >115–150%; (+) 105–115%; = , 96–104%; (–), 91–95%; –, 50–80%; – –, <50% of controls.
Shaded values indicate statistical significance at $p < 0.05$ level or higher. nd, not determined.

MITOCONDRIA y SE

- Expresion en el tiempo y distribucion espacial de Caspasa-3 despues del status epileptico experimental:contribucion de la muerte neuronal tardia secundario a injuria neuronal por convulsiones.

- **Neurobiology Diseases .2005 Apr,18(3):582-90.**

Epilepsia, 48(Suppl. 8):24–27, 2007
doi: 10.1111/j.1528-1167.2007.01341.x

The role of mitochondria in status epilepticus

Hannah Cock

Epilepsy Group, Department of Cardiac and Vascular Sciences, St. Georges, University of London and Atkinson Morley Regional Neuroscience Centre, St. Georges Hospital, London, United Kingdom

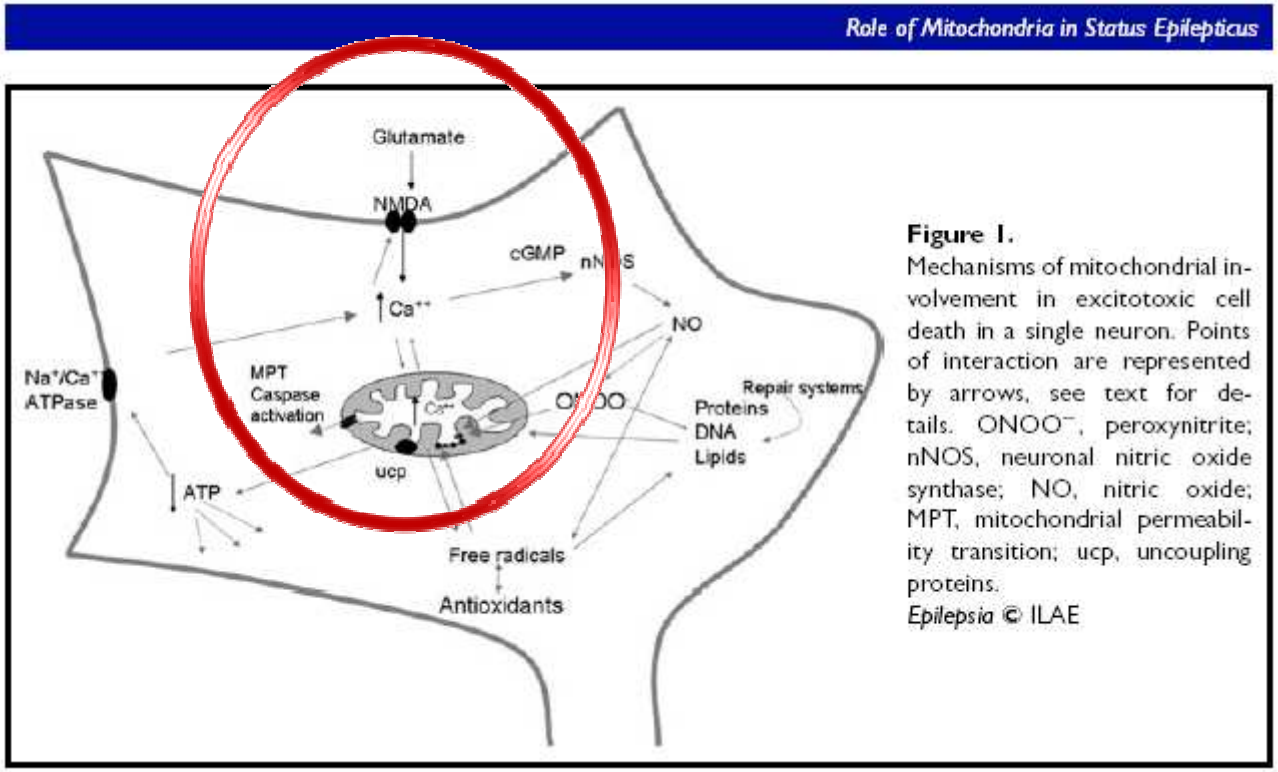


Figure 1.
Mechanisms of mitochondrial involvement in excitotoxic cell death in a single neuron. Points of interaction are represented by arrows, see text for details. $ONOO^-$, peroxynitrite; nNOS, neuronal nitric oxide synthase; NO, nitric oxide; MPT, mitochondrial permeability transition; ucp, uncoupling proteins.

El medio Ionico puede contribuir a la persistencia en el tiempo por inhibir la corriente inhibitoria mediada por GABA.
Las concentraciones de Cloro en el espacio extracelular podrian ser importantes.

Lamsa and Taira, 2003

El aumento de la permeabilidad de la Barrera Hemato Encefalica puede llevar a altos niveles de Potasio y excitación

David et al., 2009

Los procesos Inflamatorios pueden afectar la barrera hematoencefalica y perpetuar el Status.
Justificacion para el uso de Esteroides.

Tan et al., 2010

La hipotesis electrica : señala que la falla en la sincronizacion de la actividad convulsiva impediria la terminacion de las convulsiones.

Masivos cambios en la Expresion Genetica podrian ser responsables

Epilepsia, **48**(Suppl. 8):72–73, 2007
doi: 10.1111/j.1528-1167.2007.01356.x

OUTCOMES OF STATUS EPILEPTICUS

Endogenous mechanisms of neuroprotection

Roger Simon, David Henshall, Sabine Stoehr, and Robert Meller

Robert Stone Dow Laboratories, Portland, Oregon, U.S.A.

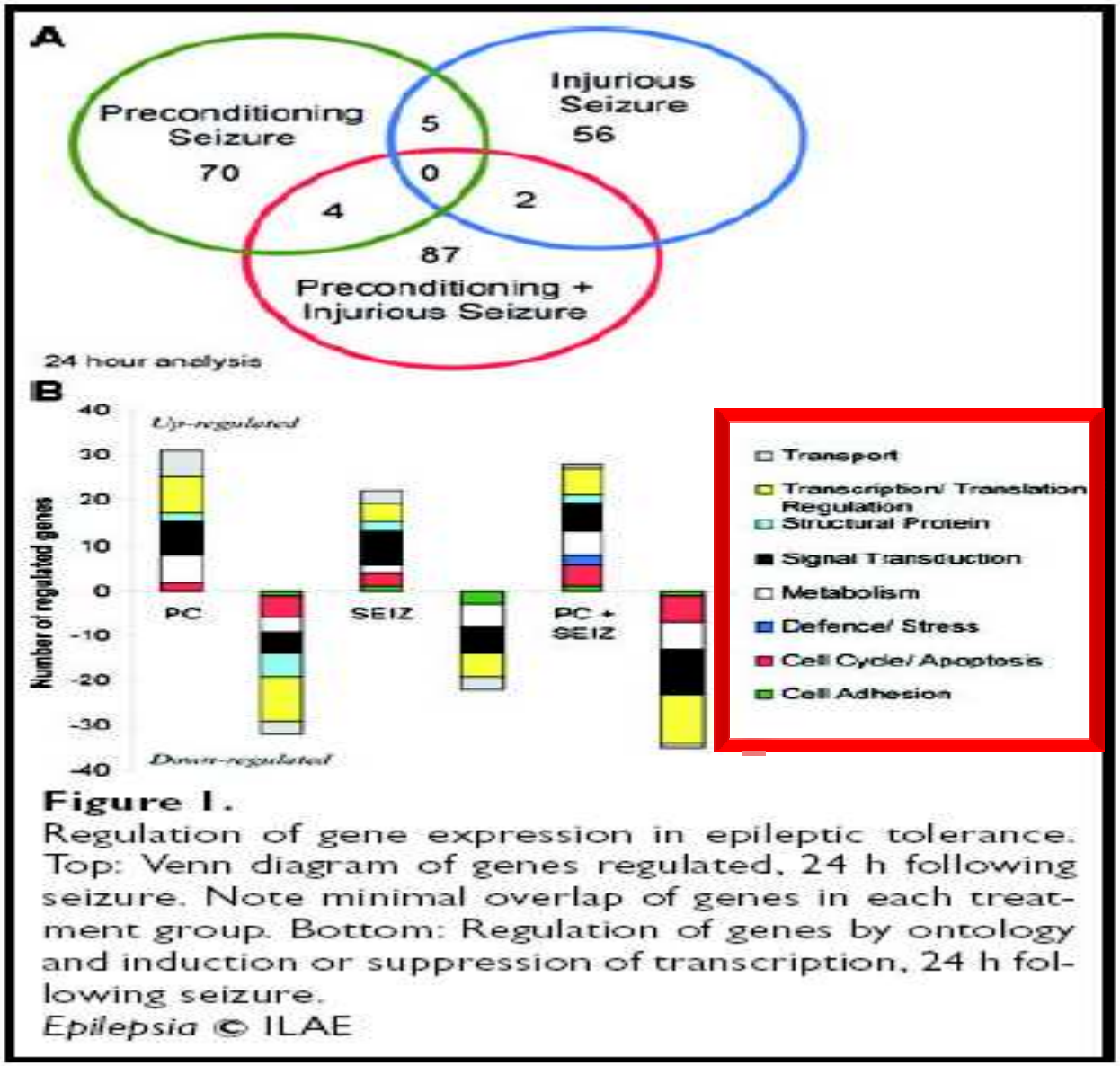
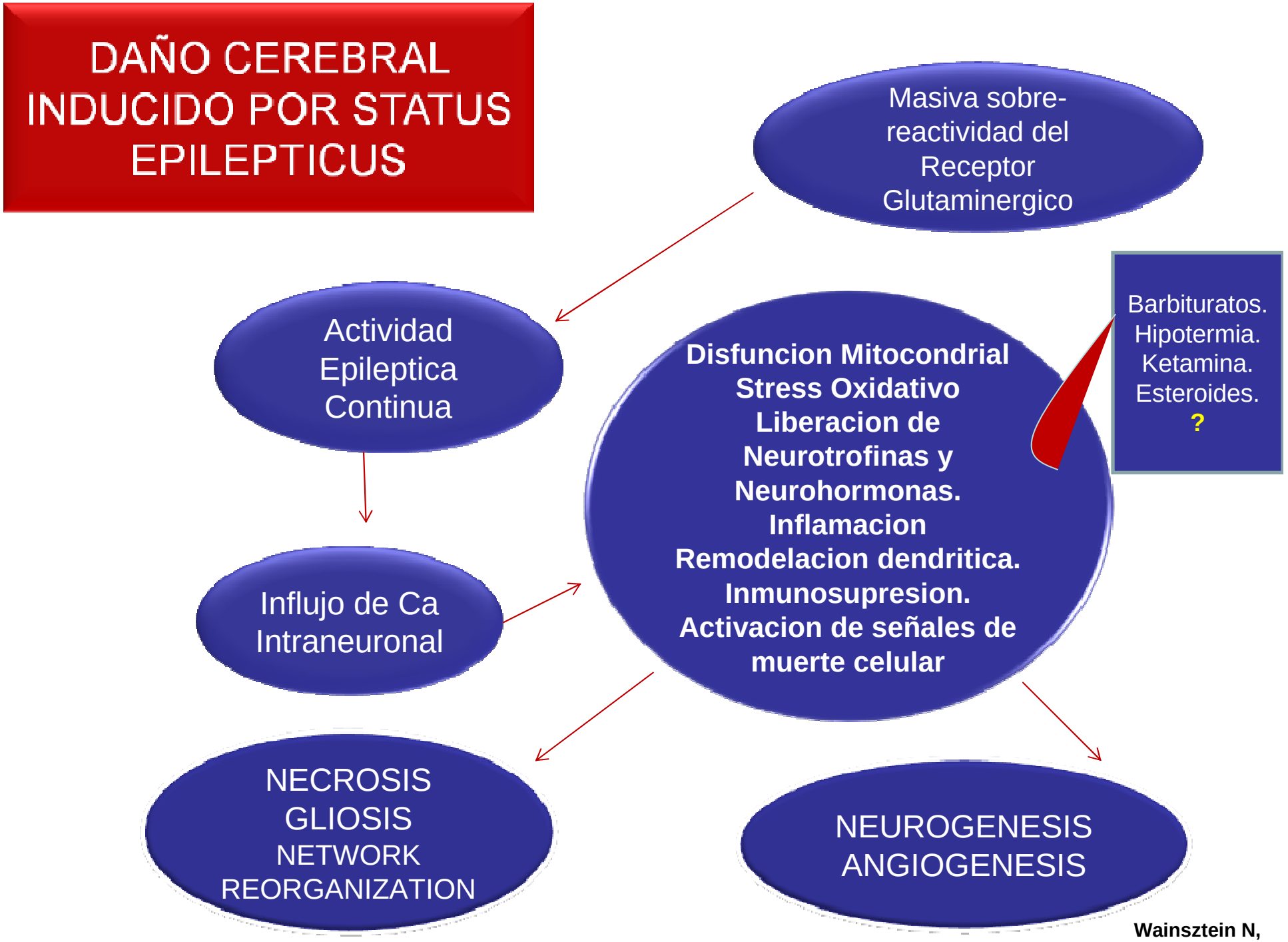


Figure 1.

Regulation of gene expression in epileptic tolerance. Top: Venn diagram of genes regulated, 24 h following seizure. Note minimal overlap of genes in each treatment group. Bottom: Regulation of genes by ontology and induction or suppression of transcription, 24 h following seizure.

DAÑO CEREBRAL INDUCIDO POR STATUS EPILEPTICUS



Wainsztein N, 2011

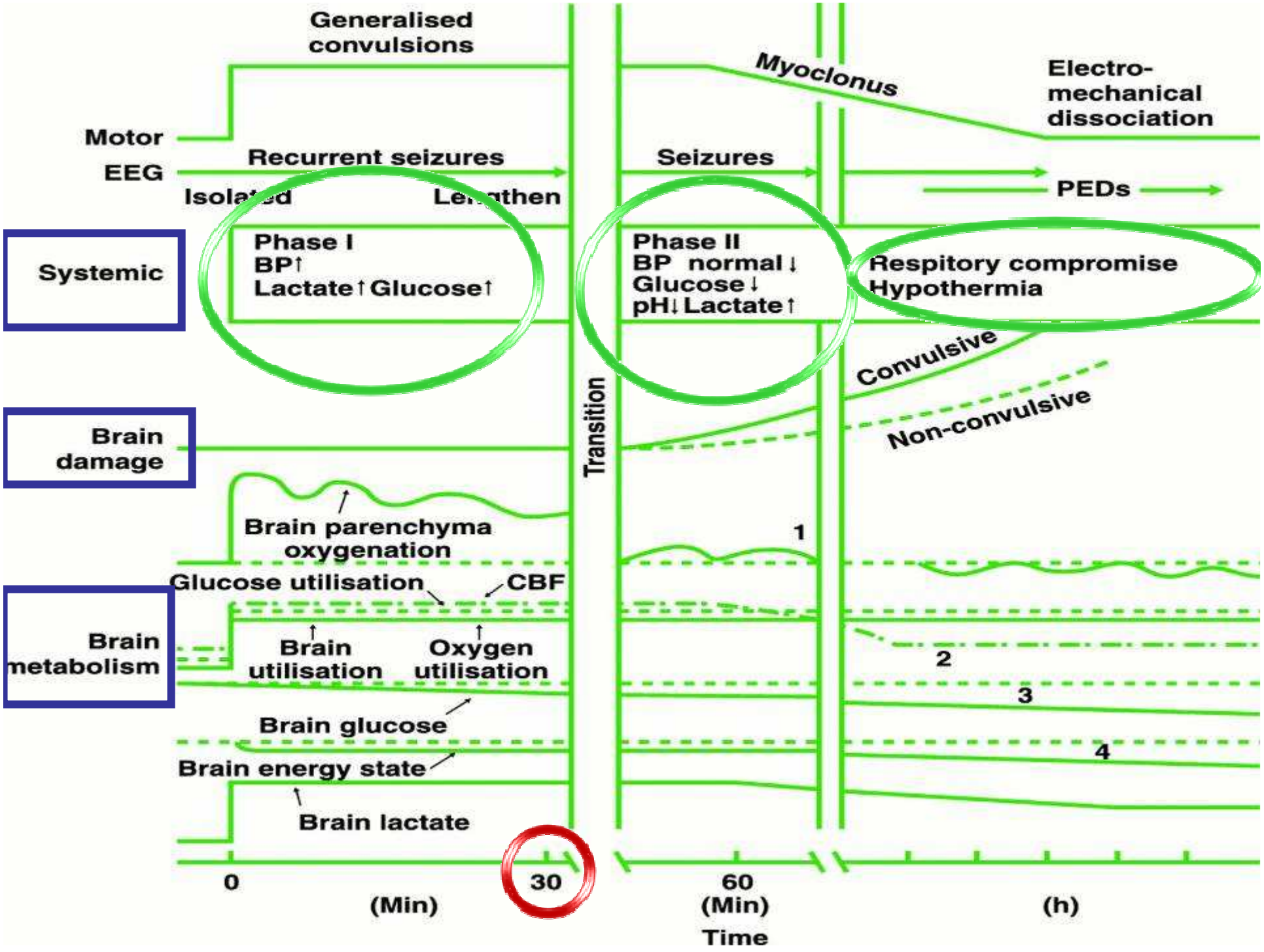
Objetivos del tratamiento del Status Epilepticus

1ero.Control de las convulsiones para interrumpir la Excitotoxicidad inicial

2do. Neuro proteccion para evitar los efectos secundarios gatillados por la Excitotoxicidad.

3ro.Evitar o Tratar las complicaciones medicas que son el resultado de la prolongada anestesia

CAMBIOS FISIOPATOLOGICOS ASOCIADOS AL STATUS EPILEPTICO


Generalised convulsions
Myoclonus
Electro-mechanical dissociation
Motor
EEG
Recurrent seizures
Seizures
PEDs
Isolated
Lengthen
Systemic
Phase I
BP↑
Lactate↑ Glucose↑
Phase II
BP normal↓
Glucose↓
pH↓ Lactate↑
Respitory compromise
Hypothermia
Convulsive
Non-convulsive
Transition
Brain damage
Brain parenchyma oxygenation
1
Glucose utilisation
CBF
Brain metabolism
Brain utilisation
Oxygen utilisation
2
3
Brain glucose
4
Brain energy state
Brain lactate
0
30
60
(Min)
(Min)
(h)
Time

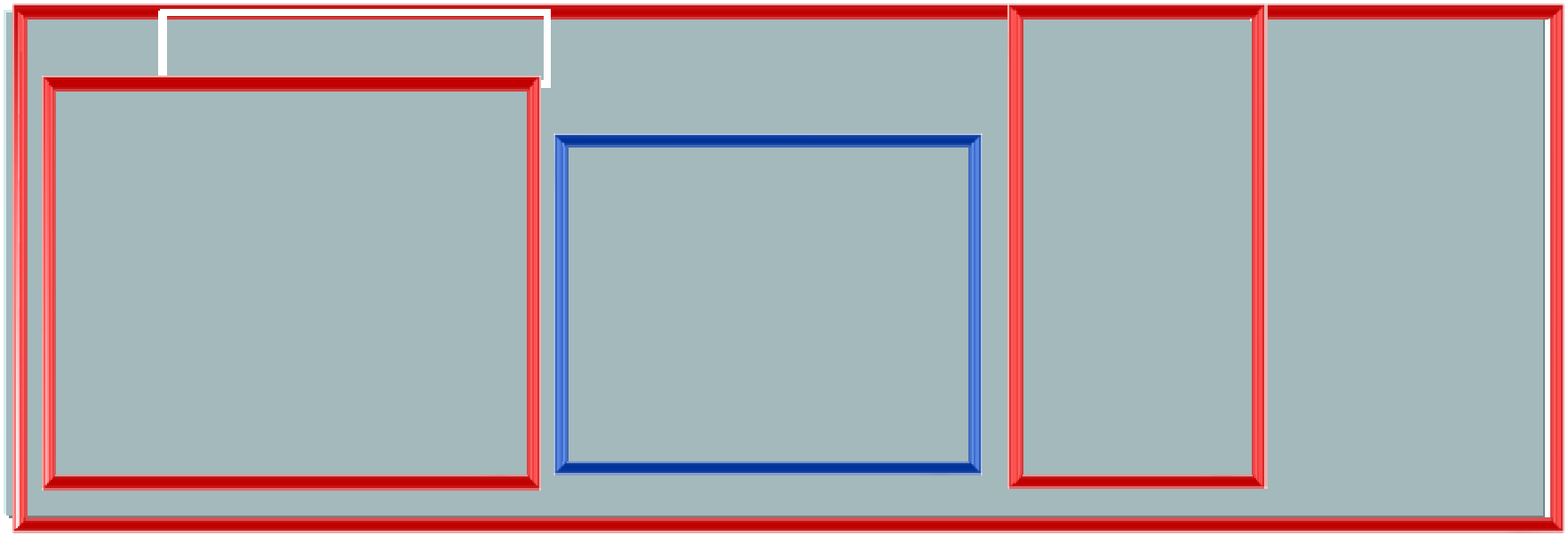
Status Epileptico

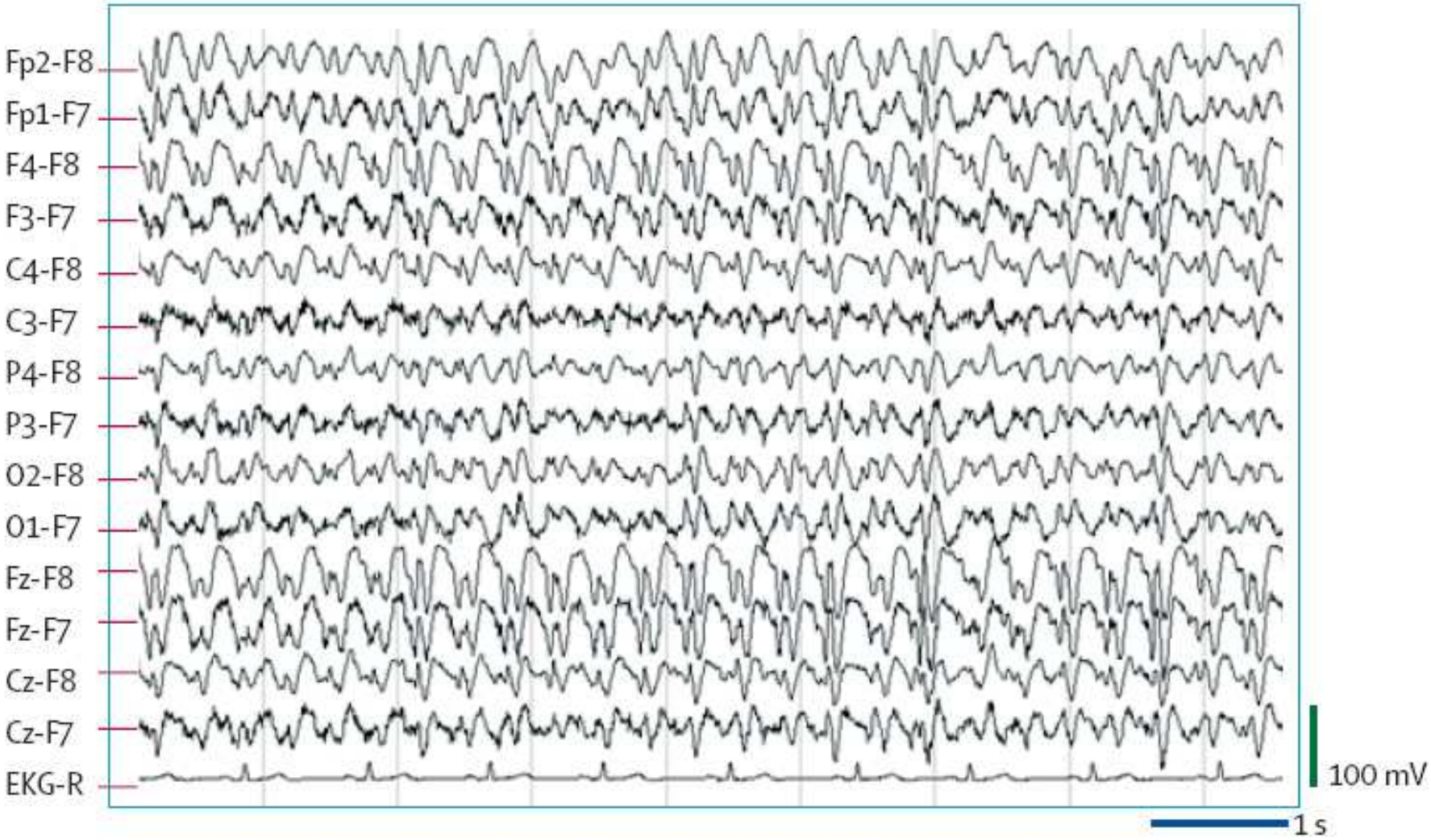
- El tratamiento consta de *cinco pilares*, que deben realizarse simultáneamente:
- Medidas generales de sostén,
- Control del status convulsivo,
- Prevención de la recurrencia,
- Corrección de la causa precipitante,
- Tratamiento de las complicaciones

Maskin P, Wainsztein N. Agosto,2010

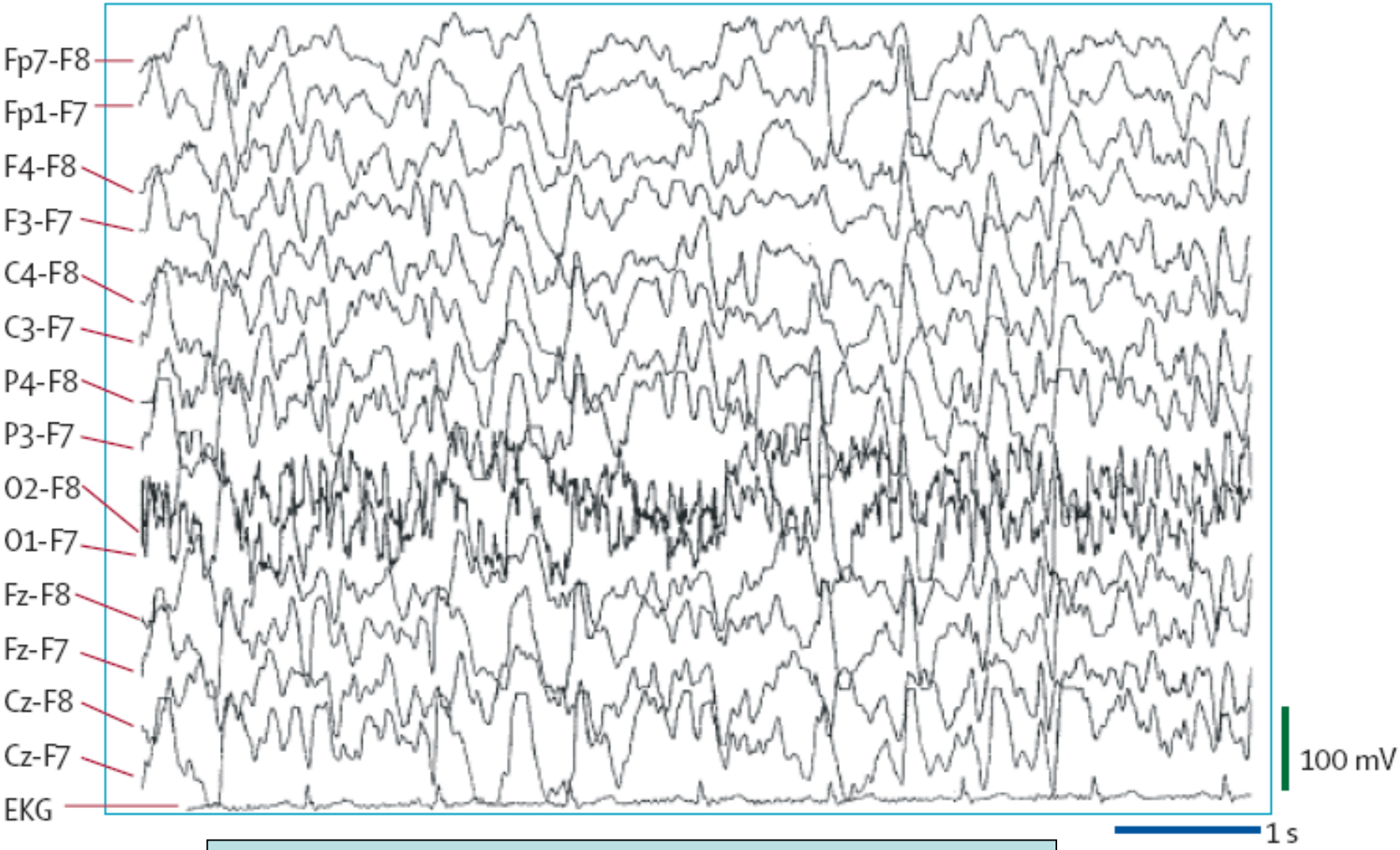
cEEG Recommendations

NCS guidelines 2012.

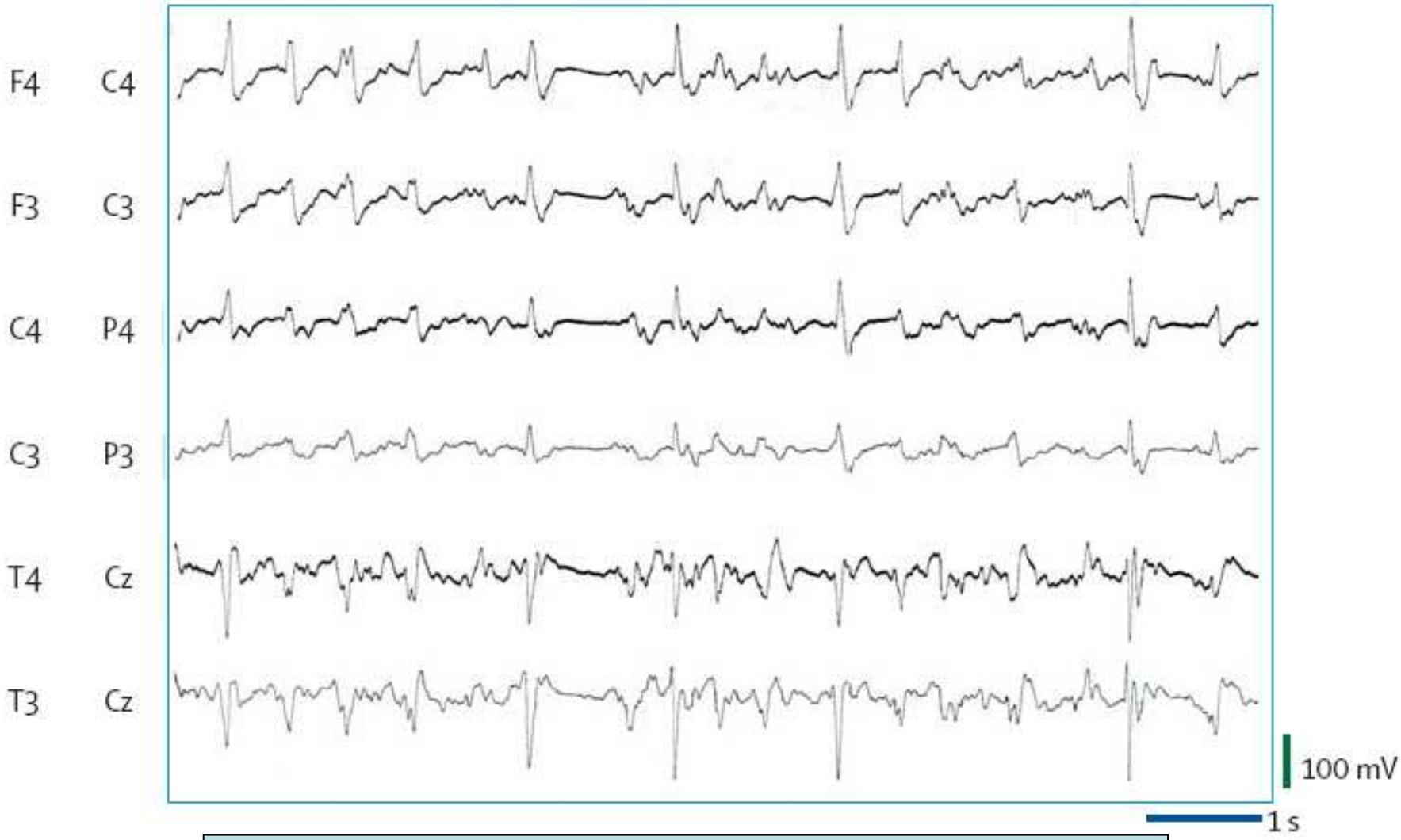




Ausencia Status Epilepticus



Parcial Complejo Status Epilepticus



Sutil Status Epilepticus

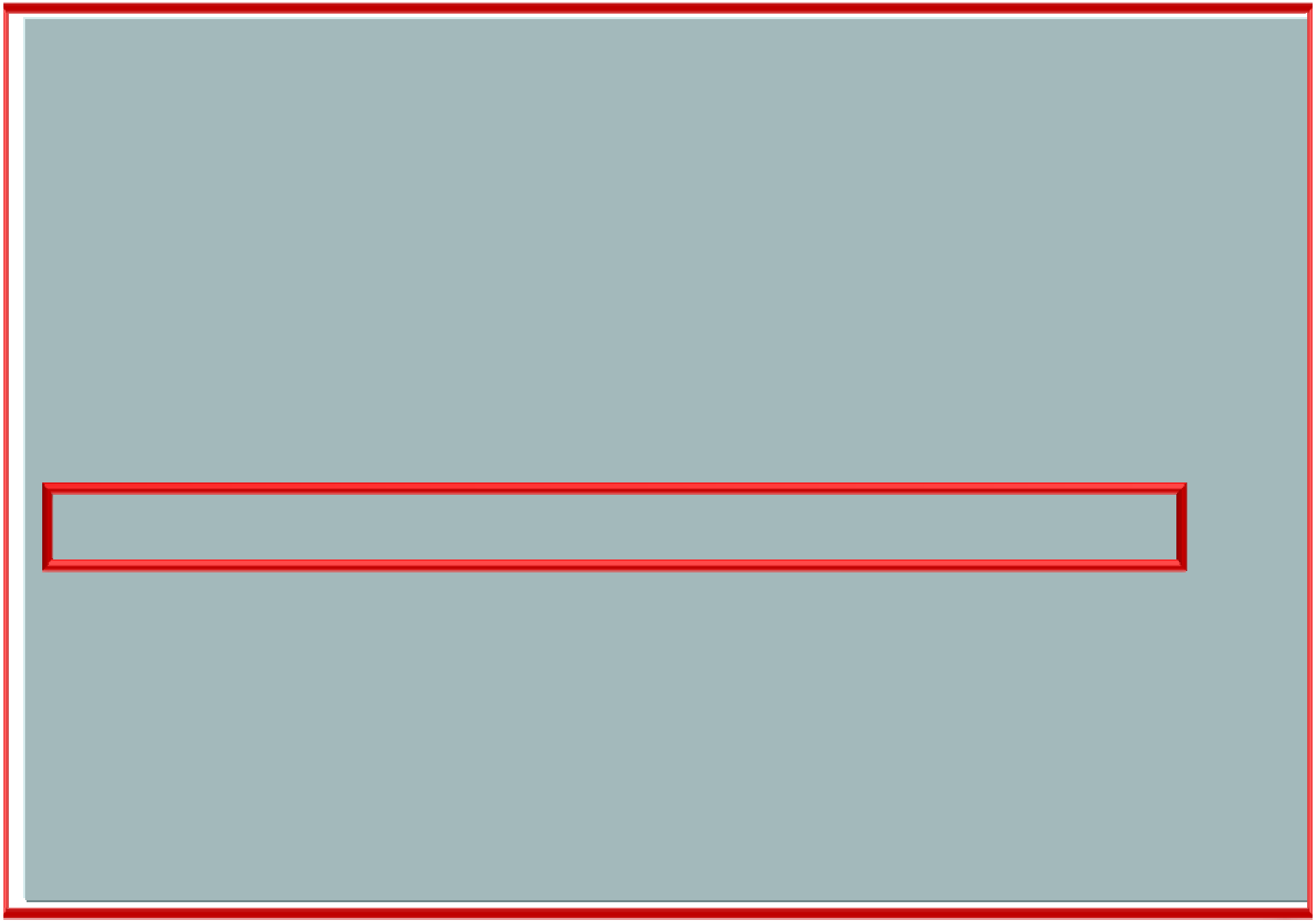
Definicion.

- Es definida como una condicion en donde la actividad epileptica es sostenida por el termino de 30 minutos o mas.
- Las convulsiones pueden tomar la forma de ataques sostenidos o la variante repetitiva de ataques:
- *SIN RECUPERACION DE LA CONCIENCIA*

Published online: 24 April 2012

Common Causes of Status Epilepticus

Antiepileptic drug noncompliance
Alcohol related
Cerebrovascular accidents
Drug toxicity (*ie*, cephalosporins, penicillins, ciprofloxacin, tacrolimus, cyclosporin, theophylline, and cocaine)
CNS infections (*eg*, meningitis and encephalitis)
CNS tumors (primary or secondary)
Metabolic disturbances (*eg*, electrolyte abnormalities, sepsis, and uremia)
Head trauma
Cerebral anoxia/hypoxia
Hypoglycemia or hyperglycemia



Alertas en la etiologia

Decrease in serum valproic acid levels during treatment with ertapenem.
Liao FF, Huang YB, Chen CY.

De novo generalised non-convulsive status epilepticus triggered by piperacillin/tazobactam.
Fernández-Torre JL, Santos-Sánchez C, Pelayo AL.

Phenytoin induced status epilepticus.
Al-Khulaif AH, Shujaa AS.

Cefepime: an underrecognized cause of nonconvulsive status epilepticus.
Lichaa H, Rachoin JS, Cerceo E, Rajput V, Surkis W.

Arch Neurol. 2010 Aug;67(8):931-40

Frequency and prognosis of convulsive status epilepticus of different causes: a systematic review.

Neligan A, Shorvon SD.

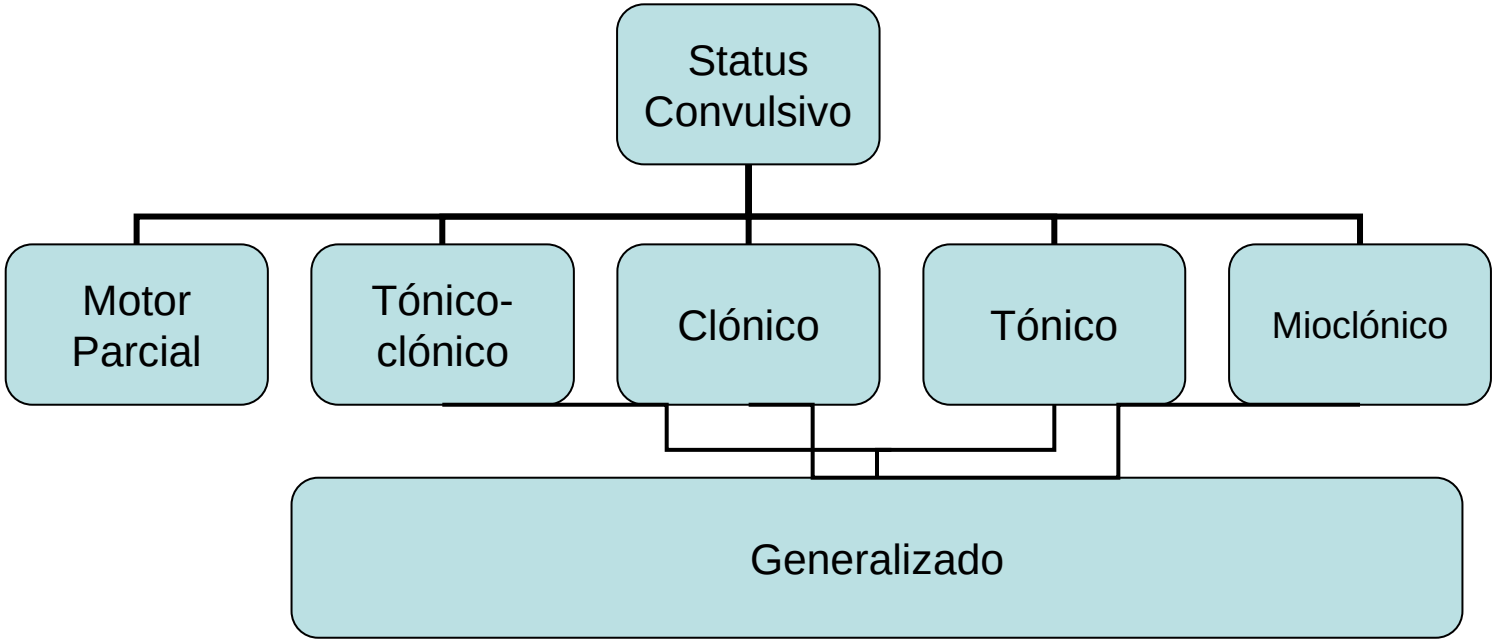
We conducted a systematic review of all studies of status epilepticus (SE) with more than 30 patients published between January 1, 1990, and December 31, 2008, to determine the frequencies of the common underlying causes and the extent to which the underlying causes affect the prognosis of an episode of SE. The frequencies of underlying causes vary among studies and show marked geographic differences, but in most studies, ***the most common underlying causes were cerebrovascular disease and low antiepileptic drug levels.***

SE de mejor pronostico.

- Niveles subterapeuticos de drogas antiepilepticas.
- Abuso de alcohol.

SE de peor pronostico

- Infeciones del SNC
- Accidente Cerebrovascular
- Encefalopatia Anoxica


Status Convulsivo
Motor Parcial
Tónico-clónico
Clónico
Tónico
Mioclónico
Generalizado

The NEW ENGLAND JOURNAL of MEDICINE

- **Current concepts in neurology: management of status epilepticus**

- A. V. Delgado-Escueta, C. Wasterlain, D. M. Treiman, and R. J. Porter

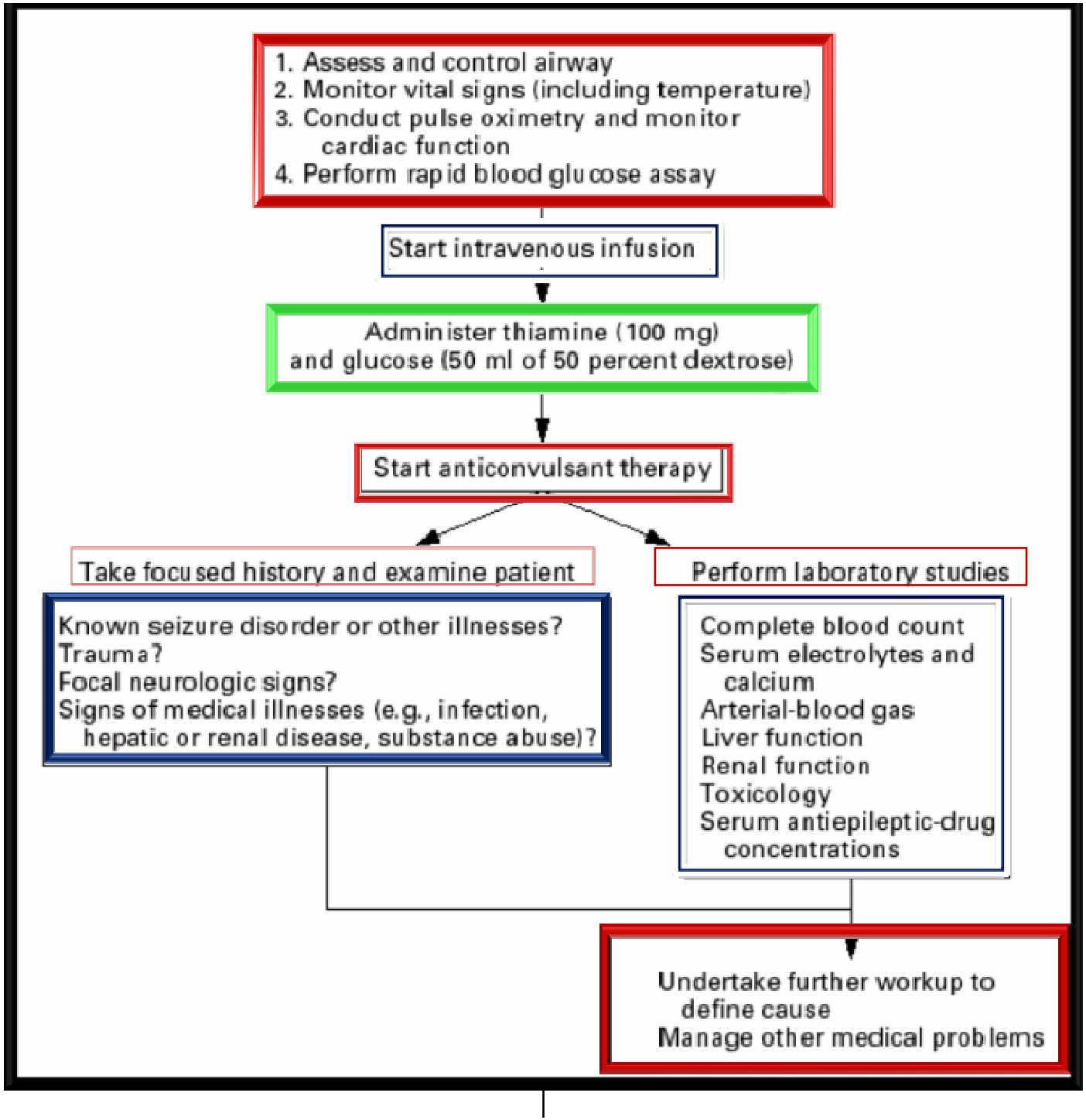
Volume 306 June 3, **1982** Number 22

SE

- Constituye una Emergencia.
- Debe resolverse idealmente dentro de los primeros 60 minutos.
- El control debe basarse en un Camino Critico.
- El paciente debe ser atendido por un especialista en Emergencias o Terapia Intensiva con la eventual ayuda del Neurologo.
- Se debe contar con EEG
- Se debe contar con dosaje de Drogas.

Manejo Inicial .
Camino Critico.
EMERGENCIAS
Los primeros 20 minutos.

- Historia Clinica Posible.
- Colocacion de via con extraccion de sangre simultanea.
- Determinacionde Glucosa Bedside
- Determinacion de NA,K,Ca,Gases, Bedside.
- Asegurar la via aerea.
- Estabilizar la Presion Arterial.
- Descender la Temperatura.
- Inicio con drogas de primera linea (Lorazepan-Diazepan-Fenitoina).


1. Assess and control airway
2. Monitor vital signs (including temperature)
3. Conduct pulse oximetry and monitor cardiac function
4. Perform rapid blood glucose assay
Start intravenous infusion
Administer thiamine (100 mg) and glucose (50 ml of 50 percent dextrose)
Start anticonvulsant therapy
Take focused history and examine patient
Known seizure disorder or other illnesses?
Trauma?
Focal neurologic signs?
Signs of medical illnesses (e.g., infection, hepatic or renal disease, substance abuse)?
Perform laboratory studies
Complete blood count
Serum electrolytes and calcium
Arterial-blood gas
Liver function
Renal function
Toxicology
Serum antiepileptic-drug concentrations
Undertake further workup to define cause
Manage other medical problems

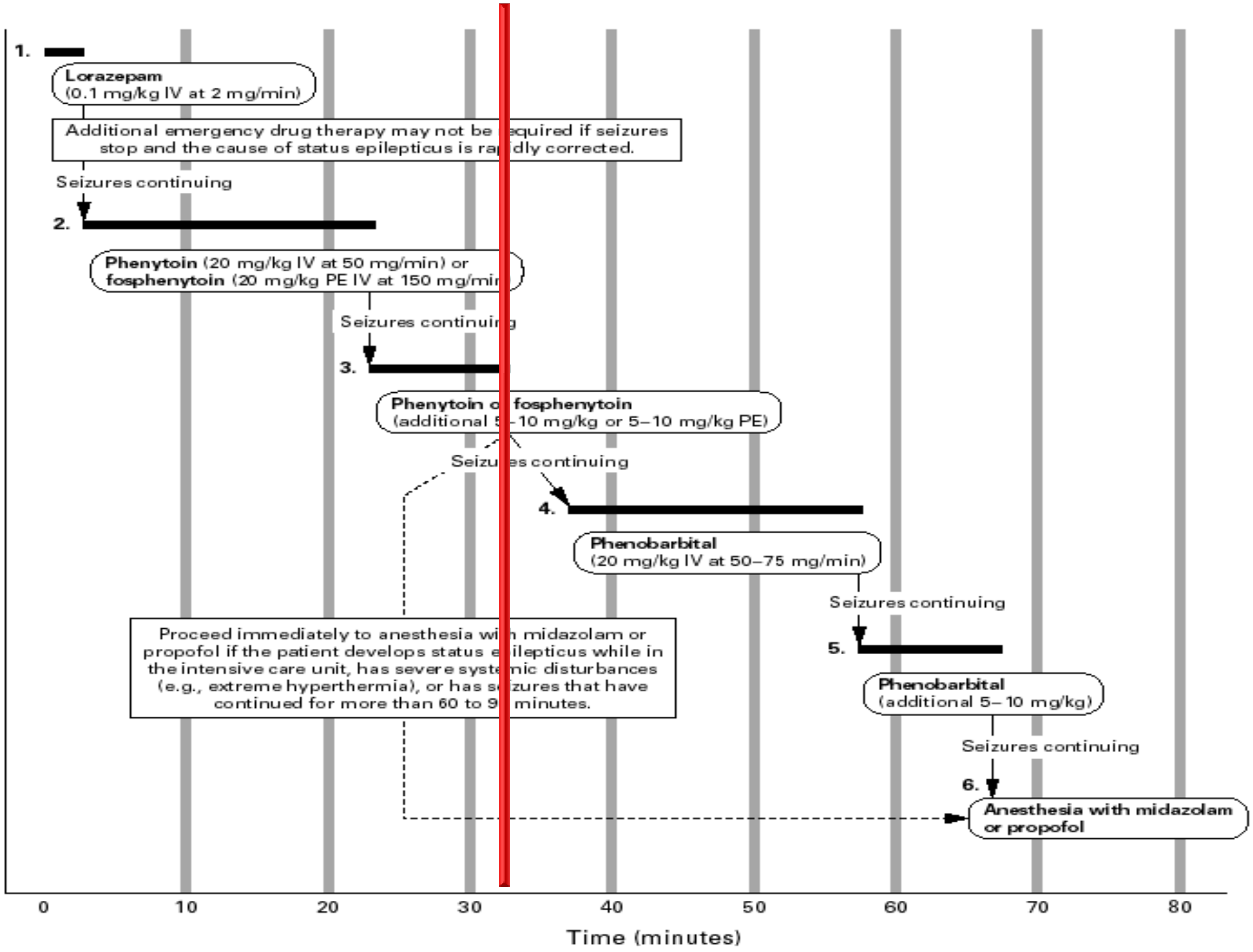

1.
Lorazepam
(0.1 mg/kg IV at 2 mg/min)
Additional emergency drug therapy may not be required if seizures stop and the cause of status epilepticus is rapidly corrected.
Seizures continuing
2.
Phenytoin (20 mg/kg IV at 50 mg/min) or
fosphenytoin (20 mg/kg PE IV at 150 mg/min)
Seizures continuing
3.
Phenytoin or fosphenytoin
(additional 5–10 mg/kg or 5–10 mg/kg PE)
Seizures continuing
4.
Phenobarbital
(20 mg/kg IV at 50–75 mg/min)
Seizures continuing
5.
Phenobarbital
(additional 5–10 mg/kg)
Seizures continuing
6.
Anesthesia with midazolam or propofol
Proceed immediately to anesthesia with midazolam or propofol if the patient develops status epilepticus while in the intensive care unit, has severe systemic disturbances (e.g., extreme hyperthermia), or has seizures that have continued for more than 60 to 90 minutes.
0
10
20
30
40
50
60
70
80
Time (minutes)

TABLE 1. Protocol for drug treatment, general measures, and emergency investigations of convulsive status epilepticus as function of time from the onset of the seizure

Prolonged epileptic seizure
Premonitory stage/out-of-hospital (nonmedical persons)

Time	Drug treatment		General measures	Emergency investigations
5 min.	Adults Diazepam 10 mg rectally	Children Diazepam 0.5 mg/kg rectally	Airway Breathing Circulation	Glucometer
	Repeat once if necessary		Safety	
	If seizure continues, proceed Early status epilepticus			

First stage/out-of or in-hospital (medical personel)

Time	Drug treatment		General measures	Emergency investigations
5 – 20 min.	Adults Lorazepam i.v. 4 mg bolus or	Children Lorazepam i.v. 0.1 mg/kg (max 4 mg) or	Airway; oxygen	Glucose, Na, K, Ca, CRP, Astrup
	Diazepam i.v. 10 mg	Diazepam i.v. 0.3 mg/kg (max 10 mg)	Cardiorespiratory function and regular monitoring; ECG, blood pressure, SpO_2 Intravenous access; i.v. glucose, thiamine, pyridoxine (children) Treat acidosis	Levels of AEDs Toxicology screening Kidney and liver function tests
	If seizure continues, proceed Established status epilepticus			

Second stage/emergency department

Time	Drug treatment	General measures	Emergency investigations
20–60 min	Fosphenytoin i.v. 15–18 mg PE/kg at max. rate of 150 mg PE/min or	Cardiorespiratory function and monitoring;	CT scan for etiology
	Phenytoin i.v. 15–18 mg/kg at max. rate of 50 mg/min	ECG, blood pressure, SpO2, use pressors if needed	CSF for CNS infection
	or in children: Phenobarbital i.v. 15–20 mg/kg at max. rate of 100 mg/min	Identify and treat medical complications	EEG for pseudostatus
	If seizure continues, proceed Refractory status epilepticus		

Third stage/intensive care unit

Time	Drug treatment	General measures	Emergency investigations
>60 min	General anesthesia	Intensive care; ventilatory and hemodynamic treatment	Continuous EEG monitoring; electrographic seizures, depth of anesthesia (burst-suppression)
	Thiopental; 3–5 mg/kg bolus, then 3–5 mg/kg/h or	Increased intracranial pressure; measure and treat if signs	Monitor
	Pentobarbital 10–15 mg/kg, then 0.5–1 mg/kg/h	Anesthesia continued for 12–24 h after last clinical or electrographic seizure	Astrup, K, Na, glucose, lactate, levels of AEDs
	or	Optimize maintenance AED treatment	
	Midazolam; 0,2 mg/kg boluses max. 2 mg/kg, then 0.05–2 mg/kg/h or only in adults: Propofol; 1–2 mg/kg boluses, max. 10 mg/kg, then 2–10 mg/kg/h		

PE, phenytoin equivalents; SpO_2, pulse oximetry. Modified from Finnish guideline.

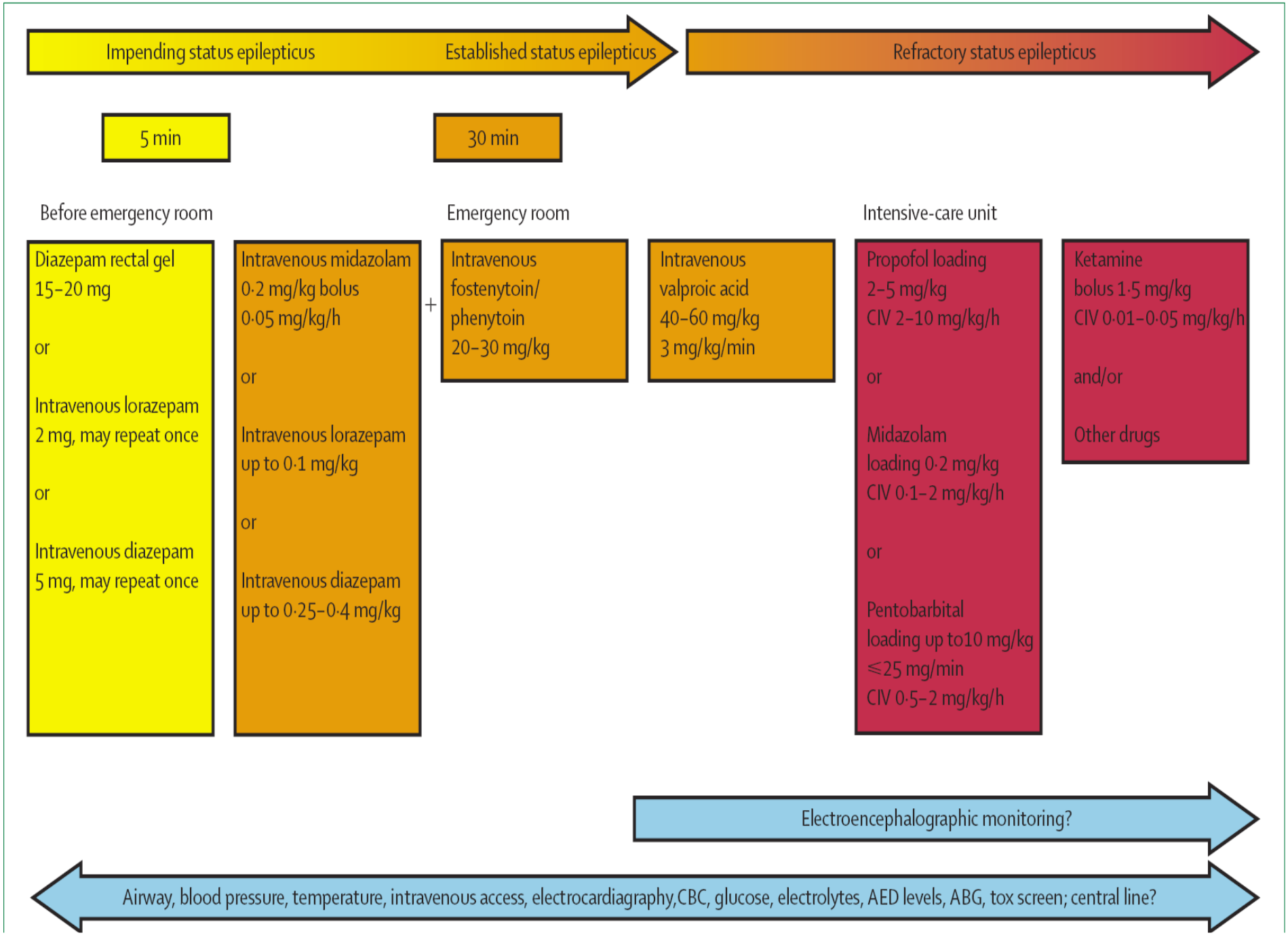
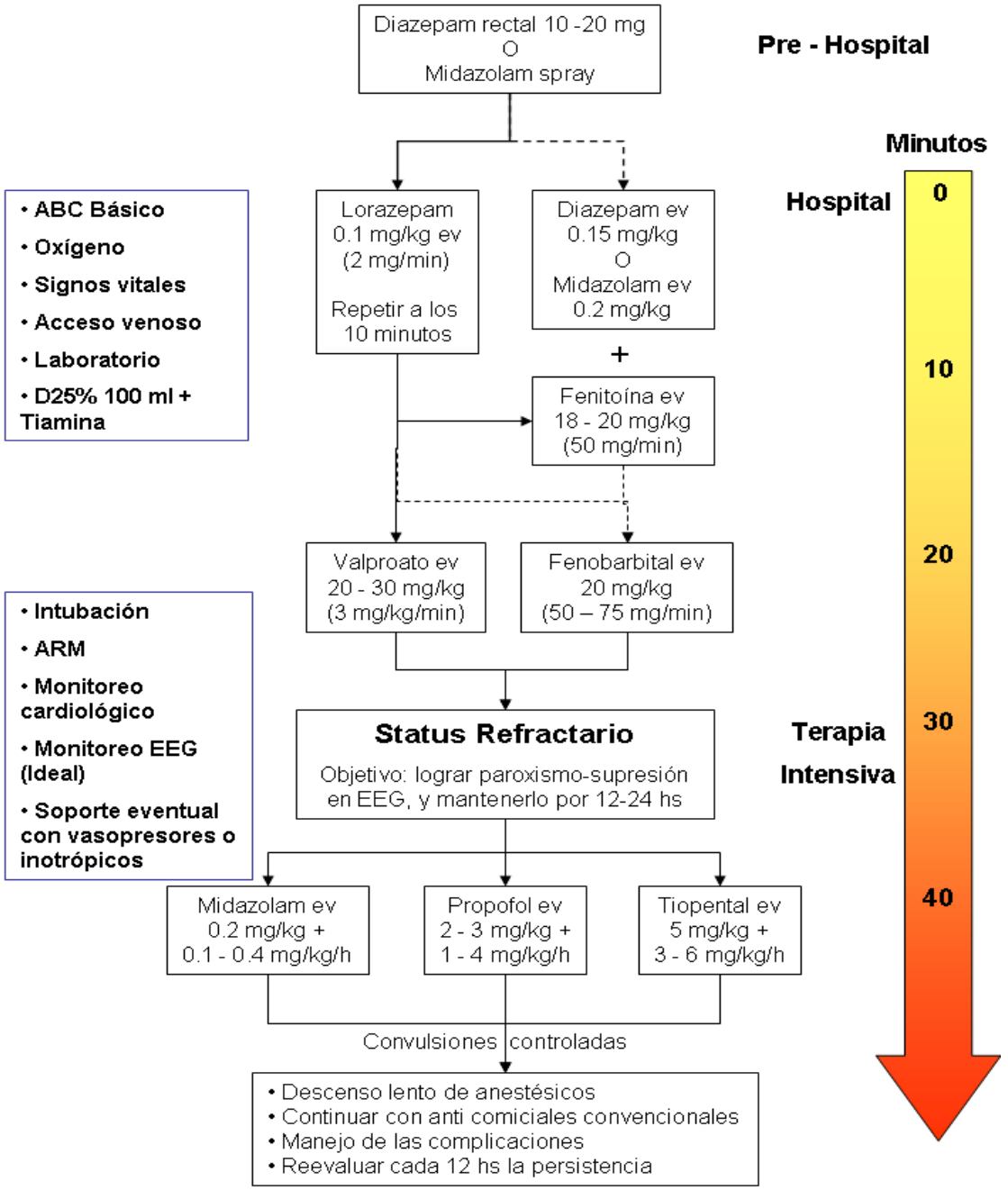

Impending status epilepticus
Established status epilepticus
Refractory status epilepticus
5 min
30 min
Before emergency room
Emergency room
Intensive-care unit
Diazepam rectal gel
15–20 mg
or
Intravenous lorazepam
2 mg, may repeat once
or
Intravenous diazepam
5 mg, may repeat once
Intravenous midazolam
0·2 mg/kg bolus
0·05 mg/kg/h
or
Intravenous lorazepam
up to 0·1 mg/kg
or
Intravenous diazepam
up to 0·25–0·4 mg/kg
+
Intravenous
fostenytoin/
phenytoin
20–30 mg/kg
Intravenous
valproic acid
40–60 mg/kg
3 mg/kg/min
Propofol loading
2–5 mg/kg
CIV 2–10 mg/kg/h
or
Midazolam
loading 0·2 mg/kg
CIV 0·1–2 mg/kg/h
or
Pentobarbital
loading up to10 mg/kg
≤25 mg/min
CIV 0·5–2 mg/kg/h
Ketamine
bolus 1·5 mg/kg
CIV 0·01–0·05 mg/kg/h
and/or
Other drugs
Electroencephalographic monitoring?
Airway, blood pressure, temperature, intravenous access, electrocardiagraphy,CBC, glucose, electrolytes, AED levels, ABG, tox screen; central line?

Figura 2 – Algoritmo



Maskin P, Wainsztein N. Agosto,2010

European Journal of Neurology 2006, **13:** e5–e6

LETTER TO THE EDITOR

Acute encephalopathy after intravenous administration of valproate in non-convulsive status epilepticus

N. Embacher, E. Karner, J. Wanschitz,
R. Beer and E. Trinka

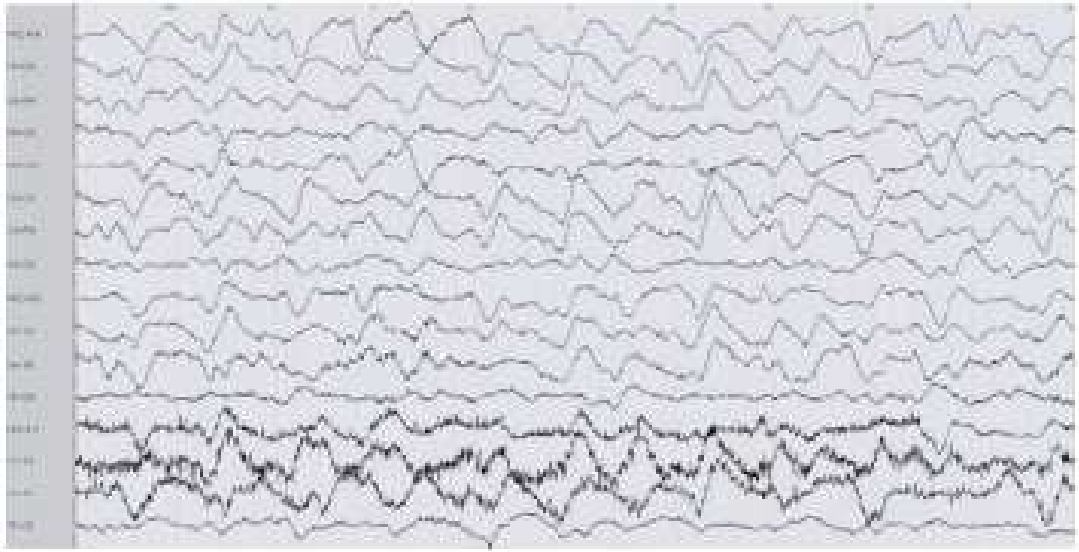


Figure 2 Electroencephalogram (EEG) on day 2 of intravenous valproat (IV VPA) therapy. EEG exhibits diffuse generalized slowing with high amplitude delta activity predominantly over the frontal regions as a consequence of VPA induced encephalopathy clinically presenting with a stuporous state, occurrence of generalized tonic clonic seizures (GTCS), repeated vomiting followed by coma.

MALAS HERRAMIENTAS ?

- Difenilhidantoina
- Fenobarbital
- Acido Valproico
- Midazolam
- Propofol
- Thiopental Sodico

Toxicidaddes multiples
Inductores Enzimaticos
Inductores de SHOCK.

La probabilidad de retornar a la linea de base despues del **Status Epileptico Refractario** es tan bajo como el **21%.**
La necesidad de rehabilitacion para los sobrevivientes del **post- Status No refractario** es **35%** y para **el post-Status Refractario del 82%** .-

Table 2. Summary of recent data regarding barbiturates, midazolam, and propofol, in the treatment of refractory SE

	Barbiturates	Propofol	Midazolam
Short-term mortality in seven recently published series (Krishnamurthy and Drislane, 1996; Stecker et al., 1998; Claassen, 2001; Prasad et al., 2001; Parviainen et al., 2002; Rossetti et al., 2004; Parviainen et al., 2006)	20–55%	26–88%	17–69%
Meta-analysis (Claassen et al., 2002)			
Mortality	48%	52%	46%
Acute failure in SE control (first 6 h of treatment)	8%	27%	20%
Breakthrough seizures (during agent's administration)	12%	15%	51%
Withdrawal seizures (<48 h after agent's discontinuation)	43%	46%	63%
Hypotension requiring vasopressors	77%	42%	30%

COMPLICACIONES MEDICAS

Cerebral

- Hypoxic/metabolic cerebral damage
- Seizure induced cerebral damage
- Cerebral oedema and raised intercranial pressure
- Cerebral venous thrombosis
- Cerebral haemorrhage and infarction

Cardiorespiratory and autonomic

- Hypotension
- Hypertension
- Cardiac failure, tachy- and bradydysrhythmia, cardiac arrest, cardiogenic shock
- Respiratory failure
- Disturbances of respiratory rate and rhythm, apnoea
- Pulmonary oedema, hypertension, embolism, pneumonia, aspiration
- Hyperpyrexia
- Sweating, hypersecretion, tracheobronchial obstruction
- Peripheral ischaemia

Epilepsy Res. 2010 Jul 20.

Autonomic and cellular mechanisms mediating detrimental cardiac effects of status epilepticus.

Bealer SL, Little JG, Metcalf CS, Brewster AL, Anderson AE.
Department of Pharmacology and Toxicology, College of Pharmacy, University of Utah, Salt Lake City, UT 84121, United States.

Abstract

Prolonged seizure activity (status epilepticus; SE) can result in increased susceptibility to lethal ventricular arrhythmias for an extended period of time followi ympathetic nervous system (SymNS) and results ir activity, and increased susceptibility to ventricular arrh and the specific arrhythmogenic substrate produced during SE are unknown. To determine if detrimental cardiac effects of SE are mediated by SymNS stimulation of the heart, we examined the effects of B-adrenergic blockade (atenolol) during seizure activity on blood pressure, heart rate, ***myocyte myofilament injury*** (cardiac troponin I, cTnI), electrocardiographic activity, and susceptibility to arrhythmias. Furthermore, we determined if SE was associated with ***altered expression of the Kv4.x potassium channels, which are critical for action potential repolarization and thereby contribute significantly to normal cardiac electrical activity.*** Lithium-pilocarpine induced SE was associated with acute tachycardia, hypertension, and cardiomyocyte damage. Arrhythmogenic alterations in cardiac electrical activity accompanied by increased susceptibility to experimentally induced arrhythmias were evident during the first 2 weeks following SE. Both were prevented by atenolol treatment during seizures. Furthermore, one and two weeks after SE, myocyte ion channel remodeling, characterized by a decreased expression of cardiac Kv4.2 potassium channels, was evident. These data suggest that the cardiac effects of prolonged and intense SymNS activation during SE induce myofilament damage and downregulation of Kv4.2 channels, which alter cardiac electrical activity and increase susceptibility to lethal arrhythmias.

myocyte myofilament injury

Metabolic and systemic

- Dehydration
- Electrolyte disturbance (especially hyponatraemia, hyperkalaemia, hypoglycaemia)
- Acute renal failure (especially acute tubular necrosis)
- Acute hepatic failure
- Acute pancreatitis

Other
▸ Disseminated intravascular coagulopathy/multi-organ failure
▸ Rhabdomyolysis
▸ Fractures
▸ Infections (especially pulmonary, skin, urinary)
▸ Thrombophlebitis, dermal injury

Neurocritical Care

Guidelines for the Evaluation and Management of Status Epilepticus

Gretchen M. Brophy[1] – , Rodney Bell[2], Jan Claassen[3], Brian Alldredge[4], Thomas P. Bleck[5], Tracy Glauser[6], Suzette M. LaRoche[7], James J. Riviello Jr.[8], Lori Shutter[9], Michael R. Sperling[2], David M. Treiman[10], Paul M. Vespa[11] and Neurocritical Care Society Status Epilepticus Guideline Writing Committee

Published online: 24 April **2012**

Status Epileptico Convulsivo

Mortalidad

Al alta: 9-21%

A 30 dias :19-27%

A 90 dias: 19%

A los diez años : 2.8%

Morbilidad

Secuela neurologica Severa : 11- 16%

Deterioro en el Status funcional: 23-26%

A los 90 dias : 39% alteracion marcada del Status funcional y 43% con buena recuperacion.

Factores asociados con pronostico pobre

Edad avanzada

Alteracion de la Conciencia

Duracion de las Convulsiones ?

Comienzo con signos neurologicos focales.

Complicaciones medicas

Tasa de mortalidad en De Novo Status en pacientes hospitalizados : 61%

En pacientes con Terapeutica Adecuada la mortalidad fue tan baja como 8%

En pacientes con: dosis insuficiente
Inadecuada ruta de administracion
Retardo innecesario entre tratamientos
Inadecuada Ventilacion
Complicaciones Medicas
Carencia de EEG para guiar el tratamiento

45%

Adherencia a un Protocolo mejoro el Control y Disminuyo la duracion de la internacion en ICU y el Htal.


NCSE

Non-convulsive status epilepticus (NCSE)

NCS.2012

NCSE

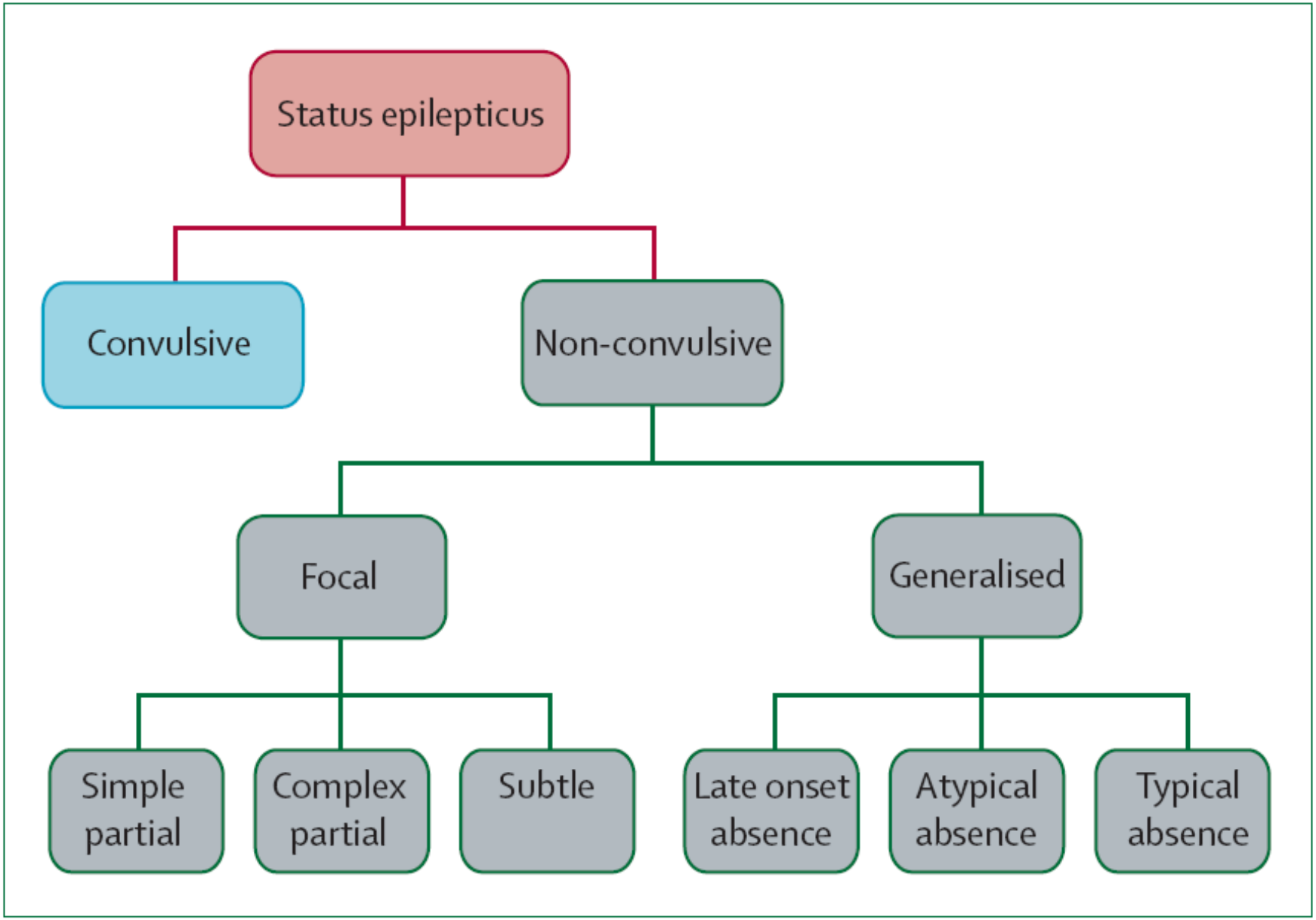
Multiple seizures or continuous seizure activity on EEG with a **nonconvulsive clinical correlate** without return to baseline state.

NCSE

Typically cognitive or behavioral change

with minor facial myoclonus

unaccompanied by frank convulsive movements



Lancet Neurol 2007; 6: 329–39

Epilepsia, **48**(Suppl. 8):85–90, 2007
doi: 10.1111/j.1528-1167.2007.01360.x

OUTCOME OF STATUS EPILEPTICUS

Cognitive outcome of status epilepticus in adults

Christoph Helmstaedter

University Clinic of Epileptology, University of Bonn, Bonn, Germany

Table 1. Ictal symptoms in nonconvulsive status epilepticus (n = 6)

Performance	Impairment
Consciousness:	Partly reduced, great fluctuations
[impaired in 4 of 6]	Never completely lost
Executive functions:	No self-initiated directed behaviors
[impaired in 6 of 6]	Preserved responsiveness, but slowed, reflexive, and restricted to single modalities preservative behaviors
	Inadequate intrusive behaviors
	Problems with concept formation & response inhibition (color/form. . .)
	Very limited working memory
Higher order functions:	Apractical signs in object use and imitation
[impaired in 6 of 6]	Receptive/expressive dysphasia
	Transcortical aphasia
	Dyscalculia
	Dyslexia
	Amnesia
	No global amnesia!
Emotion	Emotional instability [dysphoric, irritated, angry]
[changed in 4 of 6]	

Main feature: "pathological inhibition" and "negative symptoms" rater than "exitatory" and "positive" symptomatology [frontal dysexecutive?].

Panel: Differential diagnoses

Disorders mimicking non-convulsive status epilepticus

Metabolic encephalopathy

Migraine aura

Posttraumatic amnesia

Prolonged postictal confusion

Psychiatric disorders

Substance de- or intoxication

Epilepsia amnésica transitoria

Transient ischaemic attack

Lancet Neurol 2007; 6: 329–39

MORTALITY and NCSE

etiology

level of consciousness

associated comorbidities

non a particular type or pattern of EEG.

NCSE in Pacientes Criticos

Mortalidad 50 –52% en paciente criticos

Especialmente en aquellos con NCSE luego del Status Epileptico Convulsivo generalizado.

NCSE

- La Mortalidad en el grupo con epilepsia es muy bajo (1 muerte en 53 pac.-neumonia aspirativa).
- La Mortalidad en el grupo Criptogenico fue mayor quizas por la ausencia de diagnostico en problemas medicos.
- La Muerte ocurrio 39% de los pac.con alteracion severa del Status Mental y solo en el 7% sin el.
- Habitualmente los pac.comatosos tienen una enf severa ,***pero la alteracion del Status Mental en si mismo predispone a otras complicaciones.***

Epilepsia, **48**(Suppl. 8):44–45, 2007
doi: 10.1111/j.1528-1167.2007.01347.x

CLINICAL ASPECTS OF STATUS EPILEPTICUS

How urgent is the treatment of nonconvulsive status epilepticus?

Pierre Thomas

UF EEG/Epileptologie, Service de Neurologie, Hôpital Pasteur, Nice, France

NCSE

Mortalidad

Al alta: 18- 52%

A los 30 dias: 65%

Factores asociados a Pobre evolucion despues del NCSE

Etiologia subyacente

Alteracion severa del Status mental

Duracion prolongada de la convulsion

Pacientes diagnosticados dentro de los 30 minutos : mortalidad 36%

Pacientes diagnosticados a mas de 24 hs: mortalidad 75%

Pacientes con NCSE resueltos dentro de las 10 hs: mortalidad 10/%

Pacientes con NCSE resueltos mas alla de las 20 hs : mortalidad 85%

Pacientes con causa conocida : mortalidad al alta 3 %

Pacientes con causa desconocidad : mortalidad al alta 27%

NCSE

SE RECOMIENDA UN MANEJO MENOS AGRESIVO????

Nonconvulsive Status Epilepticus after Subarachnoid Hemorrhage

Neurosurgery 51:1136-1144, 2002

CONCLUSION: cEEG monitoring detected NCSE for 8% of patients with SAH and otherwise unexplained coma or neurological deterioration. The seizures were highly refractory to therapy, and the prognosis for these patients was extremely poor. Routine postoperative cEEG monitoring of patients with SAH who are at high risk for NCSE, allowing earlier diagnosis and treatment, offers the best chance of improving the outcomes for patients with this disorder.

Neurosurgery 51:1136-1144, 2002

Eur Neurol. 2005 Jul 5;54(1):10-13

Prognosis following Postanoxic Myoclonus Status epilepticus.

Hui AC, Cheng C, Lam A, Mak V, Jouvet GM

Postanoxic Myoclonus Status epilepticus

90 % de MORTALIDAD

Prediction implications. In general, de nosis. The prese of myoclo ctor. We report series of pa which was define as continu 18 patients were retrieved, oped a mean of 11.7 h afte lied following MSE and the 2 survivors were highly dependent or remained in a persistent vegetative state, supporting the view that prognosis is poor in this condition. Copyright (c) 2005 S. Karger AG, Basel.

Neurology. 2005 Jul 26;65(2):314-6.

Clinical features of status epilepticus in patients with HIV infection.

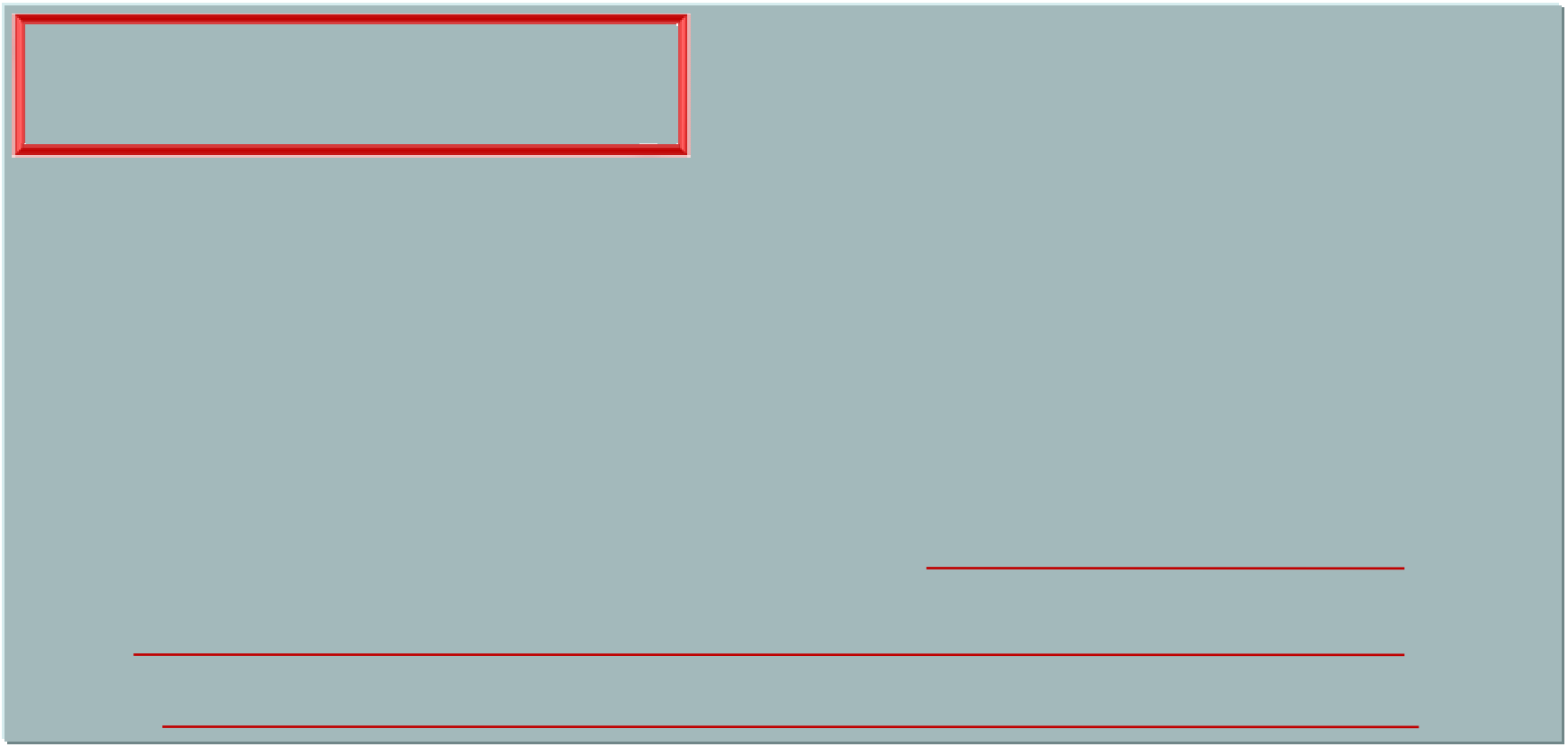
Lee KC, **Garcia PA**, **Alldredge BK**.

The authors reviewed the records of 42 patients with HIV infection and status epilepticus (SE) ***Brain tumor and infection were the most common etiologies***. The median duration of SE was 2.0 +/- 10 hours. Most patients (37 [88%]) responded to IV benzodiazepine or phenytoin treatment.

29% patients died

36% developed new neurologic deficits.

In patients with HIV infection, aggressive management of seizures may limit the risk of SE.



Status Epiletico Refractario

Mortalidad

Al alta: 23-61%

A los 3 meses: 39%

En niños : de muy baja a 32%

En niños : mortalidad de 20% en sintomaticos y 4% en idiopaticos

Morbilidad

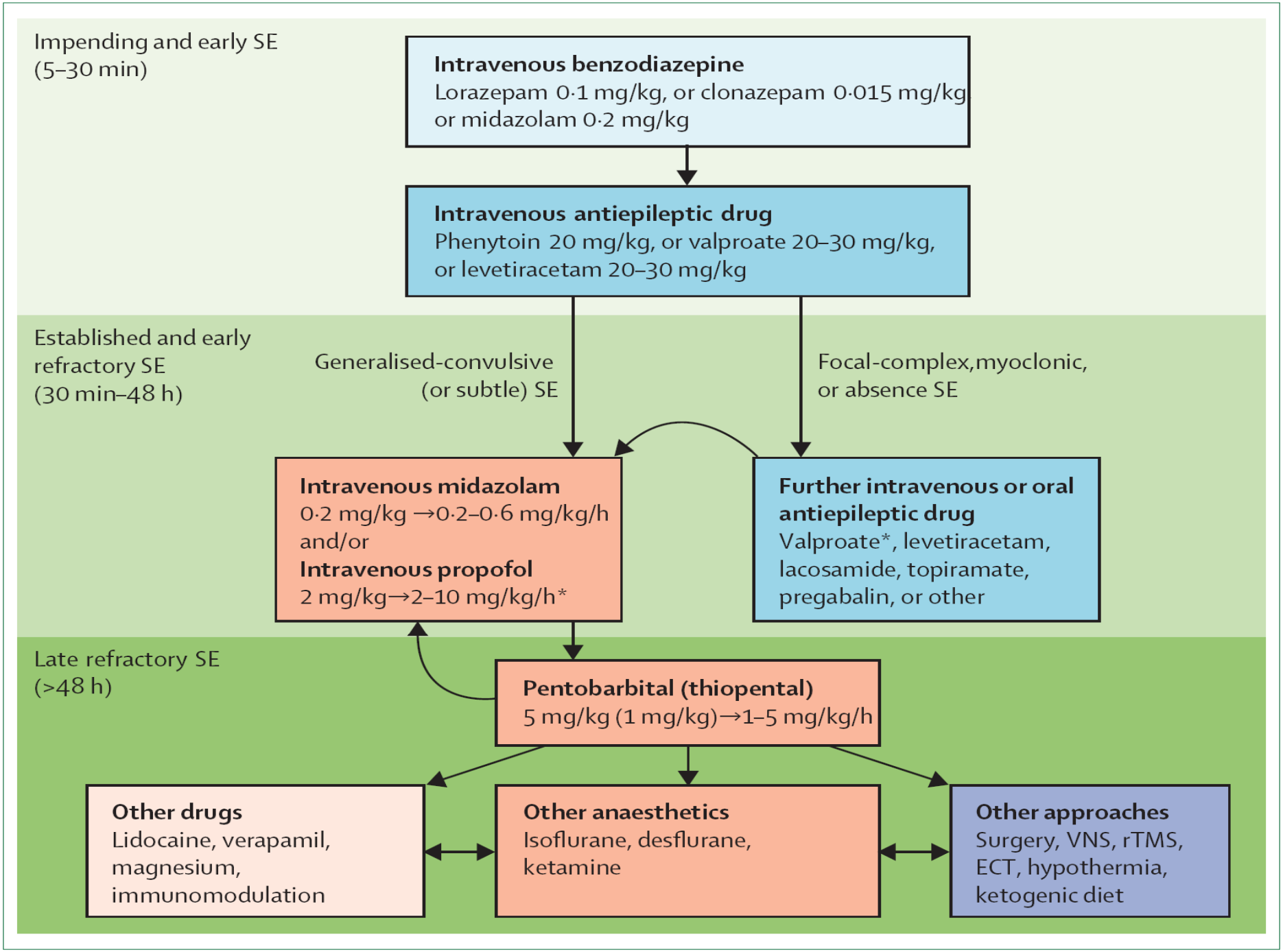
Retornal a la linea de base es mas frecuente en el SE que en el RSE y se ha visto en el 39%.

Epilepsia post SE es mas frecuente de ser vista en los sobrevivientes a largo plazo de RSE (88%) que en aquellos con SE no refractario (22%)

Management of refractory status epilepticus in adults: still more questions than answers

Andrea O Rossetti, Daniel H Lowenstein

Lancet Neurol 2011; 10: 922–30


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
Intravenous antiepileptic drug
Phenytoin 20 mg/kg, or valproate 20–30 mg/kg,
or levetiracetam 20–30 mg/kg
Established and early
refractory SE
(30 min–48 h)
Generalised-convulsive
(or subtle) SE
Focal-complex,myoclonic,
or absence 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*
Further intravenous or oral
antiepileptic drug
Valproate*, levetiracetam,
lacosamide, topiramate,
pregabalin, or other
Late refractory SE
(>48 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

Factores asociados a Pobre evolucion del RSE

Etiologia subyacente

Edad avanzada (mayor de 50 años)

Larga duracion de las convulsiones

Coma

Tipo de SE

APACHE 2 : elevado

Duracion no asociada a la evolucion??

BRAIN
A JOURNAL OF NEUROLOGY

REVIEW ARTICLE

The treatment of super-refractory status epilepticus: a critical review of available therapies and a clinical treatment protocol

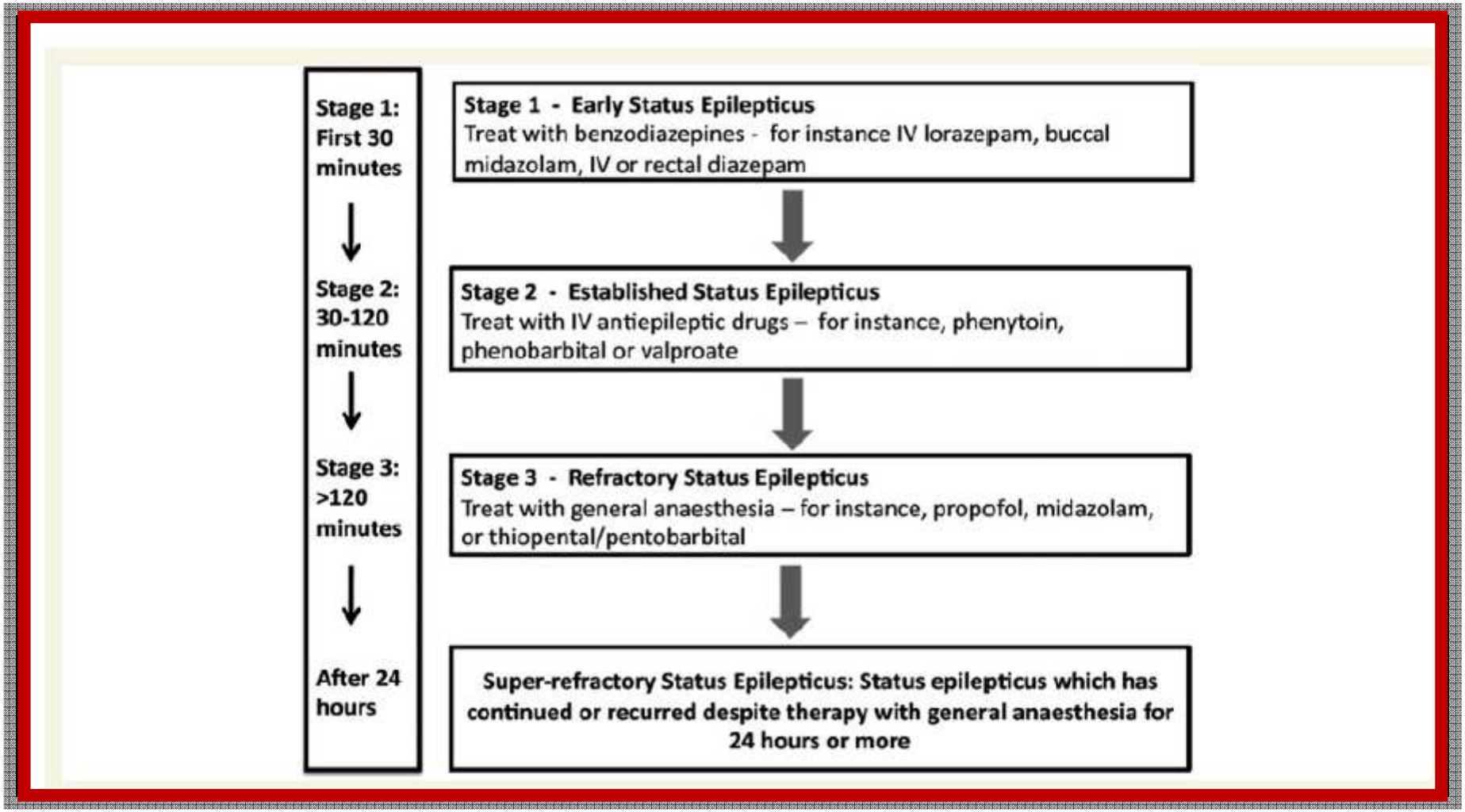
Simon Shorvon and Monica Ferlisi

BRAIN,October 2011;134(10)2802-2818

Status -Epilepticus Super - Refractario

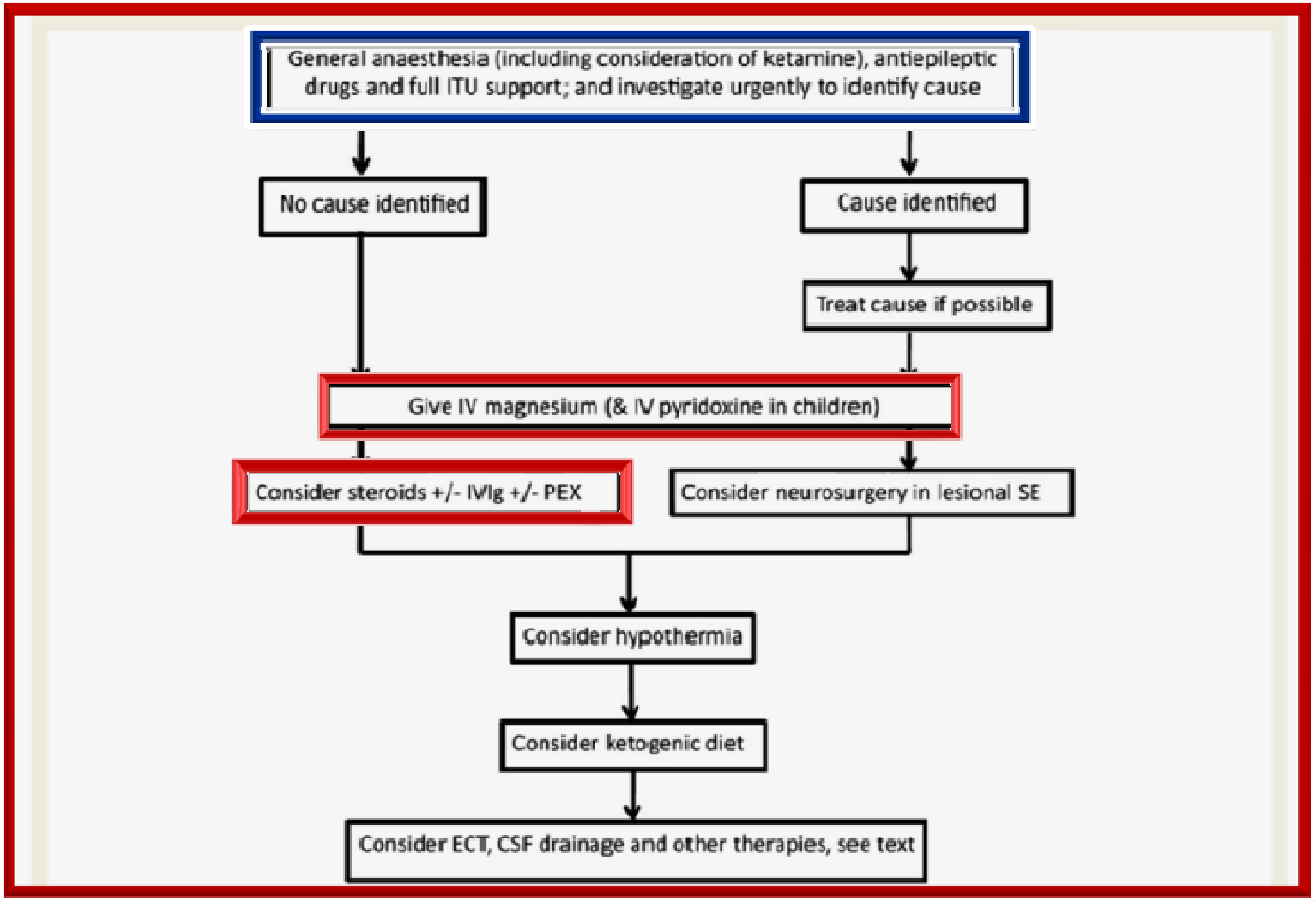
Es el Status Epilepticus que continua o recurre a las 24 horas o mas despues del comienzo de la terapeutica anestesica, incluyendo los casos que recurren en la reduccion o retiro de la anestesia.

Shorvon and Trinka. Third London-Innsbruck Colloquium on status epilepticus. Oxford 7-9 April ,2011.



BRAIN,October 2011;134(10)2802-2818

Status Epilepticus Super-Refractario



BRAIN,October 2011;134(10)2802-2818

OTRAS OPCIONES TERAPEUTICAS.

	Advantages	Disadvantages/comments
Isoflurane[71]		
Ketamine[72–75]		
Lidocaine[76,77]	Can rescue phenytoin-resistant refractory status epilepticus	Cardiac monitoring needed; possible seizure induction
Verapamil[78,79]	Safe	Does not have antiepileptic drug action; might improve availability of antiepileptic drugs in CNS
Magnesium[80]		
Ketogenic diet[81,82]		
Immunological treatments[83]	Can act causally	Formal exclusion of infection needed before treatment
Piridoxina		

11 casos reportados

17 casos reportados

Anon 1995. RCT : Eclampsia – antiNMDA/ POLG1 deficit

Antiinflamatorio?

Mutacion de ALDH 7ª .14 pac en 5 reportes.SE in pregnancy

Lancet Neurol 2011; 10: 922–30

	Advantages	Disadvantages/comments
Resective surgery[101]		ticus; gical risks
Vagal nerve stimulation[102]	Appropriate for long-term use	Invasive procedure; cardiac arrhythmias rarely reported
Repetitive transcranial magnetic stimulation[103]	Non-invasive procedure	Possible seizure induction; need for sustained treatment
Electroconvulsive treatment[104,105,106]	Non-invasive procedure	Need for skilled interdisciplinary team; possible seizure induction
Mild hypothermia[107]	Acts on several mechanisms	barbiturates
Classical music[108]	No known side-effects	Based on one case series

36 PACIENTES EN 15 REPORTS

10 reportes de casos

Lancet Neurol 2011; 10: 922–30

Emergent Initial Therapy

Treatment	Class/level of evidence	References
Emergent treatment		
Lorazepam	Class I, level A	[19, 30, 52, 83, 87–98]
Midazolam	Class I, level A	[84, 99–108]
Diazepam	Class IIa, level A	[30, 87, 90, 95, 97–105, 107, 109–114]
Phenytoin/fosphenytoin	Class IIb, level A	[30, 87, 94, 115–119]
Phenobarbital	Class IIb, level A	[30, 87, 114]
Valproate sodium	Class IIb, level A	[116, 117, 120–122]
Levetiracetam	Class IIb, level C	[119, 123–130]

Urgent treatment

Valproate sodium	Class IIa, level A	[117, 120–122, 131–136]
Phenytoin/fosphenytoin	Class IIa, level B	[30, 87, 97, 107, 114, 115, 117, 119, 132, 133, 137]
Midazolam (continuous infusion)	Class IIb, level B	[106]
Phenobarbital	Class IIb, level C	[138, 139]
Levetiracetam	Class IIb, level C	[119, 123, 125–127, 129, 133, 140, 141]

Refractory treatment

Midazolam	Class IIa, level B	[28, 106–108, 142–150]
Propofol	Class IIb, level B	[26, 36, 62, 66, 68, 144, 151–155]
Pentobarbital/thiopental	Class IIb, level B	[26, 27, 56, 58, 59, 62, 63, 66, 68, 107, 115, 139, 154, 156–158]
Valproate sodium	Class IIa, level B	[120, 121, 131, 136, 159–161]
Levetiracetam	Class IIb, level C	[37, 66, 125–127, 129, 140, 141, 159, 162–164]
Phenytoin/fosphenytoin	Class IIb, level C	[57, 165]
Lacosamide	Class IIb, level C	[166–168]
Topiramate	Class IIb, level C	[169]
Phenobarbital	Class IIb, level C	[138]

Drug	Initial dosing	Administration rates and alternative dosing recommendations	Serious adverse effects	Considerations
Diazepam	0.15 mg/kg IV up to 10 mg per dose, may repeat in 5 min	Up to 5 mg/min (IVP) Peds: 2–5 years, 0.5 mg/kg (PR); 6–1 years, 0.3 mg/kg (PR); greater than 12 years, 0.2 mg/kg (PR)	Hypotension Respiratory depression	Rapid redistribution (short duration), active metabolite, IV contains propylene glycol
Lorazepam	0.1 mg/kg IV up to 4 mg per dose, may repeat in 5–10 min	Up to 2 mg/min (IVP)	Hypotension Respiratory depression	Dilute 1:1 with saline IV contains propylene glycol
Midazolam	0.2 mg/kg IM up to maximum of 10 mg	Peds: 10 mg IM (>40 kg); 5 mg IM (13 40 kg); 0.2 mg/kg (intranasal); 0.5 mg/kg (buccal)	Respiratory depression Hypotension	Active metabolite, renal elimination, rapid redistribution (short duration)
Fosphenytoin	20 mg PE/kg IV, may give additional 5 mg/kg	Up to 150 mg PE/min; may give additional dose 10 min after loading infusion Peds: up to 3 mg/kg/min	Hypotension Arrhythmias	Compatible in saline, dextrose, and lactated ringers solutions
Lacosamide	200–400 mg IV	200 mg IV over 15 min No pediatric dosing established	PR prolongation Hypotension	Minimal drug interactions Limited experience in treatment of SE
Levetiracetam	1,000–3,000 mg IV Peds: 20–60 mg/kg IV	2–5 mg/kg/min IV		Minimal drug interactions Not hepatically metabolized
Phenobarbital	20 mg/kg IV, may give an additional 5–10 mg/kg	50–100 mg/min IV, may give additiona dose 10 min after loading infusion	Hypotension Respiratory depression	IV contains propylene glycol
Phenytoin	20 mg/kg IV, may give an additional 5–10 mg/kg	Up to 50 mg/min IV; may give addition dose 10 min after loading infusion Peds: up to 1 mg/kg/min	Arrhythmias Hypotension Purple glove syndrome	Only compatible in saline IV contains propylene glycol
Topiramate	200–400 mg NG/PO	300–1,600 mg/day orally (divided 2–4 times daily) No pediatric dosing established	Metabolic acidosis	No IV formulation available
Valproate sodium	20–40 mg/kg IV, may give an additional 20 mg/kg	3–6 mg/kg/min, may give additional dose 10 min after loading infusion Peds: 1.5–3 mg/kg/min	Hyperammonemia Pancreatitis Thrombocytopenia Hepatotoxicity	Use with caution in patients with traumatic head injury; may be a preferred agent in patients with glioblastoma multiforme

Urgent control AED therapy recommendations include use of :

IV fosphenytoin/phenytoin,

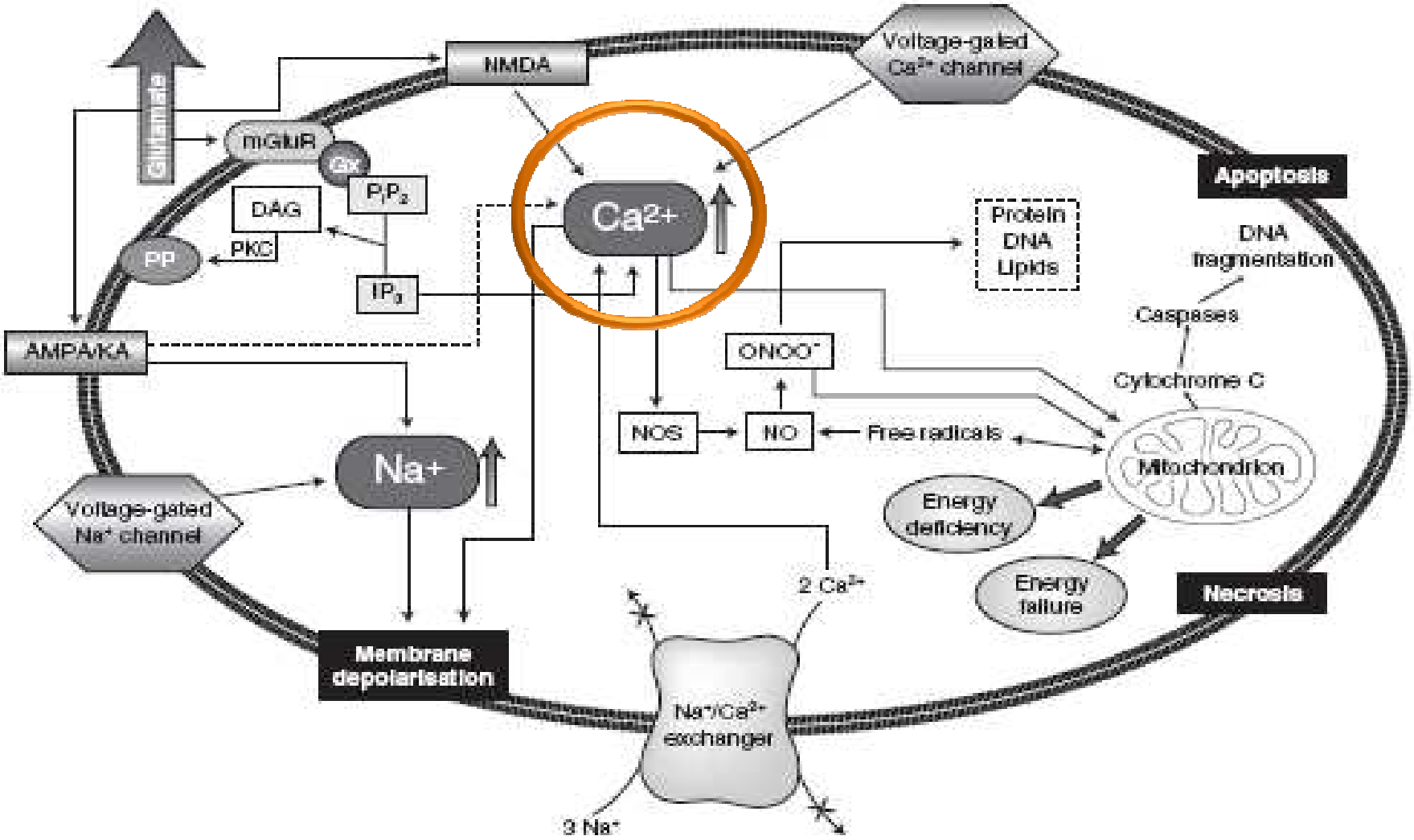
valproate sodium

or levetiracetam

(*strong recommendation, moderate quality*).

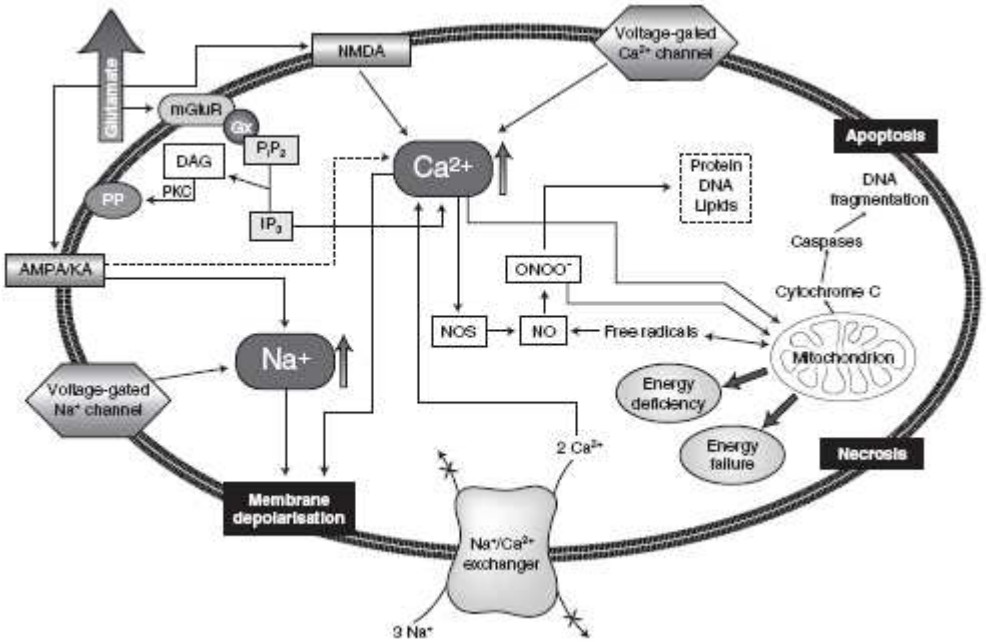
Neurocritical Care 2012

Inhibe canales Ca++ alto voltaje tipo N-
Reduce liberación de Ca++ de depósitos Intraneuronales-
Unión a prot. SV2A en vesículas presinápticas (afecta transmisión sináptica y gabaérgica)



LEVETIRACETAM: MECANISMO DE ACCION EFECTOS NEUROPROTECTORES

- Inhibe canales Ca++ alto voltaje tipo N- Reduce liberación de Ca++ de depósitos Intraneuronales- Unión a prot. SV2A en vesículas presinápticas (afecta transmisión sináptica y gabaérgica)



*Modelo experimental (injuria craneal severa y HSA) : Lev se asoció a mejoría en la recuperación funcional y reducción del vasoespasmo. Este efecto no se evidenció con DFH o fosfenitoína
Neurocritical Care, 2006; 05: 71-78

•Efecto neuroprotector en infartos cerebrales
•Seizure, 2001;10-287

•Up regulation producción astrocítica de NO (inducción sintasa NO)
Brain Res: 2003, 976 (2): 227

METABOLISMO

- Levetiracetam no se metaboliza extensamente en humanos.
- *La vía metabólica principal (24 % de la dosis) es la hidrólisis enzimática del grupo acetamida.*
- La formación del metabolito primario, ucb L057, no está soportada por las isoformas del citocromo P450 hepático.
- La hidrólisis del grupo acetamida fue mesurable en un gran número de tejidos, incluyendo las células sanguíneas.
- El metabolito ucb L057 es farmacológicamente inactivo.
- Se identificaron también dos metabolitos minoritarios.
- Otros compuestos no identificados representaban solamente el 0,6 % de la dosis

• Levetiracetam

- *100% de absorcion oral e intercambiable a la via EV*
- *No hepatotóxica. Ajusta en IR (66%)*
- *Concentr.pico: 1.3 hs- Meseta: a las 48 horas*
- *No interacción en cit P450*
- *Interaccion ? carbamacepina y topiramato*
- *Cinética lineal.*
- *Concentraciones plasmáticas predecibles y proporcionales a dosis.*
- *No requiere dosaje.*
- *Ajuste por respuesta clínica*
- *Novel mecanismo de accion*

Estudios comparativos Levetiracetam vs DFH

- **Eficacia y tolerabilidad de levetiracetam vs DFH luego de cirugía supratentorial:**

- Retrospectivo 105 pacientes LEVETIRACETAN vs 210 DFH
- (mayoría tumores cerebrales)

No diferencias significativas en la incidencia de convulsiones a 7 y 30 días y epilepsia a los 12 meses.

Hubo más reacciones adversas (requirió cambio de medicación)

1/ 105 (levetiracetam) vs 38 / 210 (difenilhidantoína)

Persistencia de la medicación al año: Levetiracetam (64 %) DFH (26 %)

Neurology® 2008;71:665-669

LEVETIRACETAM: seguridad y eficacia

- Aprobado por FDA en 1999: convulsiones de comienzo parcial con o sin generalización y tratamiento adjunto de mioclonías y convulsiones generalizadas (status) . Utilizada frecuente en unidades neuroquirúrgicas como profilaxis.

- En pacientes críticos ha demostrado eficacia en prevención y recurrencia de convulsiones (82 a 93 %) con bajo nivel de efectos adversos. (aunque no usó Monitoreo continuo)

Epilep & Behav, 2008-12:477 (droga EV)

Neurocritical Care, 2009(11) 34 (droga EV y oral

EFECTOS ADVERSOS:

- Somnoliencia (14 vs 8,4 %)
- Astenia
- Mareos dificultad coordinación
- Trastornos de comportamiento y psiquiatricos
- Hematológicos : trombocitopenia leve. . 1 caso de aplasia.
- ***Menor incidencia de SUDEP***

- *LOS EFECTOS ADVERSOS EN GENERAL SON LEVES Y NO REQUIEREN DISCONTINUACION* Exp. Opinion Drug Safety: 2007.6(3) 241

Levetiracetam: seguridad y eficacia : estudio observacional

Neurocrit Care (2007) 7:140–147

- La DFH usada previo a la admisión en la unidad neurocrítica fue reemplazada frecuentemente por levetiracetam
- Pacientes en Lev menos efectos adversos y menor estadía
- *Droga bien tolerada en población anciana*

Table 3 AED therapy prior to and during stay in the NSICU, by type of complication ($N = 358$)

Complication	Total	AED therapy							
		PHT monotherapy		LEV monotherapy		LEV in combination		Other AED(s)	
		Pre-NSICU	In NSICU	Pre-NSICU	In NSICU	Pre-NSICU	In NSICU	Pre-NSICU	In NSICU
Hypotension	7 (2.0)	2 (6.9)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	6 (5.5)	2 (4.2)	0 (0.0)
Encephalopathy	89 (24.9)	8 (27.6)	40 (24.0)[a]	1 (20.0)	0 (0.0)	1 (16.7)	37 (33.9)[a,b]	8 (16.7)	12 (17.9)[b]
Toxicity	44 (12.3)	6 (20.7)	21 (12.6)[c]	0 (0.0)	2 (13.3)	0 (0.0)	19 (17.4)[d]	4 (8.3)	2 (3.0)[cd]
Rash	7 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	7 (6.4)	0 (0.0)	0 (0.0)
Agitation	27 (7.5)	3 (10.3)	11 (6.6)	0 (0.0)	0 (0.0)	0 (0.0)	8 (7.3)	4 (8.3)	8 (11.9)
Acute renal failure	4 (1.1)	0 (0.0)	0 (0.0)	1 (20.0)	0 (0.0)	0 (0.0)	4 (3.7)	1 (2.1)	0 (0.0)
Liver failure	2 (0.6)	1 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.8)	0 (0.0)	0 (0.0)
Bleeding	10 (2.8)	0 (0.0)	3 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	7 (6.4)	0 (0.0)	0 (0.0)
Thrombocytopenia	21 (5.9)	2 (6.9)	3 (1.8)[e]	1 (20.0)	1 (6.7)	0 (0.0)	15 (13.8)[e,f]	1 (2.1)	2 (3.0)[f]
Other	212 (59.2)	12 (41.4)	104 (62.3)[g,h]	3 (60.0)	4 (26.7)[g,i,j]	2 (33.3)	55 (50.5)[h,i,k]	28 (58.3)	49 (73.1)[j,k]

DFH: asociación con trastornos cognitivos y peor evolución neurológica

- Evidencia Experimental: **DFH empeora recuperación funcional en Stroke**

Brailowsky S, Knight RT, Efron R. Phenytoin increases the severity of cortical hemiplegia in rats. Brain Res 1986;376:71-77.

Mecanismos de acción:

Meador KJ: Neurodevelopmental effects of antiepileptic drugs. **Current Neurol Neurosci Rep 4:**373–378, 2002

- ***DFH: reduce irritabilidad neuronal: disminución de sinaptogénesis***

Brain Pathol 2002;12:488-498.

Zubkov AY, Tibbs RE, Aoki K, Zhang JH: Morphological changes of cerebral penetrating arteries in a canine double hemorrhage model. **Surg Neurol 54:**212–220, 2000

- **Apoptosis de células endoteliales: agravamiento del vasoespasmo**

DFH: asociación con trastornos cognitivos y peor evolución neurológica

Neurocritical care 2009;10:222-224

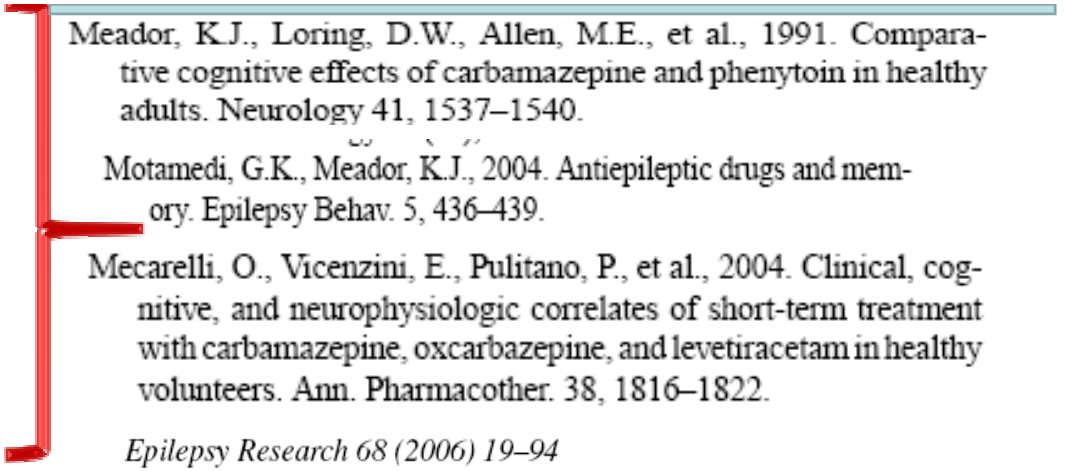
Brain Injury 2001; june 25;(6)634-637

En pacientes con Injuria cerebral la DFH puede producir resultado desfavorable en los test de atención, memoria y lenguaje.

- El uso de DFH y Carbamazepina en pacientes con epilepsia determina déficit en los test psicológicos.
- En voluntarios sanos, existe alteración en los test cognitivos y de comportamiento.
- Existe demostracion de que el uso de DFH se asocia mayor duración de amnesia post traumática
- La DFH es metabolizada por el Citocromo P450 2C9.

La enzima 2C9 exhibe polimorfismo génico en un 34,7% de las personas caucásicas (resultando en acumulación y toxicidad)

Efectos neurocognitivos de viejas drogas anticonvulsivantes



Meador, K.J., Loring, D.W., Allen, M.E., et al., 1991. Comparative cognitive effects of carbamazepine and phenytoin in healthy adults. Neurology 41, 1537–1540.

Motamedi, G.K., Meador, K.J., 2004. Antiepileptic drugs and memory. Epilepsy Behav. 5, 436–439.

Mecarelli, O., Vicenzini, E., Pulitano, P., et al., 2004. Clinical, cognitive, and neurophysiologic correlates of short-term treatment with carbamazepine, oxcarbazepine, and levetiracetam in healthy volunteers. Ann. Pharmacother. 38, 1816–1822.

Epilepsy Research 68 (2006) 19–94

- En estudios realizados en *voluntarios sanos* las viejas drogas AEs, se han asociado a *efectos cognitivos desfavorables* (trastornos en la memoria, test cognitivos y neuropsicológicos) Drogas evaluadas: CBZ, DFH, Fenobarbital y valproico

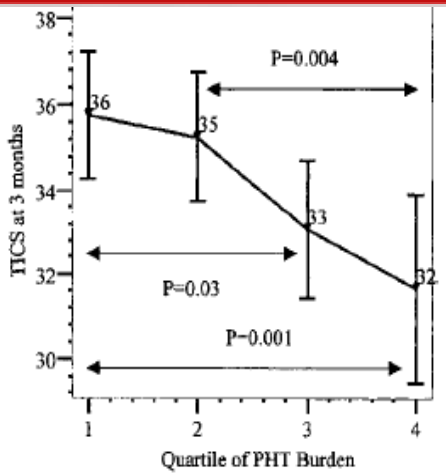
- Nuevas drogas (gabapentin, lamotrigina, oxcarbacepina, topiramato y levetiracetam) menos efectos adversos

- Levetiracetam es efectiva en el control de las convulsiones con mejoría en los test cognitivos (MMSE) y test neuropsicológicos.

Epilepsy & Behavior, 2009

Evidencia en humanos: DFH asocia a mala evolución neurológica (evidencia retrospectiva)

- 527 pacientes ***se evaluó la recuperación funcional (test Rankin mayor o igual a 4) y la evaluación cognitiva a los 14 días y 3 meses, en relación a la carga de exposición a DFH*** (promedio de dosajes de DFH X número de días entre primera y última determinación: máximo de 14 días)
- *DFH : asoció a peor evolución neurológica a los 14 días (OR:1,5 por cuartilo) tendencia no significativa a los 3 meses (multivariable e* independiente)



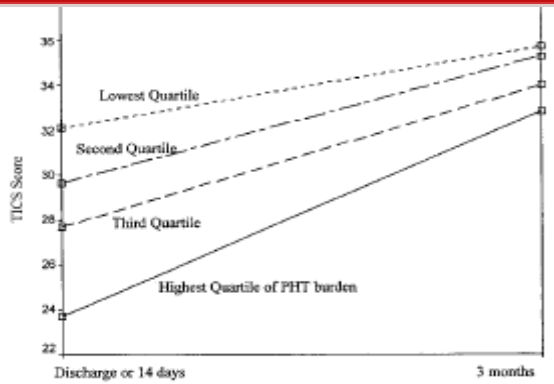


Figure 2. Change in TICS scores from hospital discharge (or 14 days) to 3 months. In all quartiles of PHT burden, TICS scores improved, but they improved faster over time in patients with higher quartile of PHT burden ($P=0.004$).

(*Stroke*. 2005;36:583-587.)

Outcome in patients with subarachnoid hemorrhage treated with antiepileptic drugs

J. Neurosurg. / Volume 107 / August, 2007

- 3552 pacientes (4 estudios randomizados doble ciego placebo control) 162 centros – 21 países (1991-1997)
- Comparó pacientes tratados.

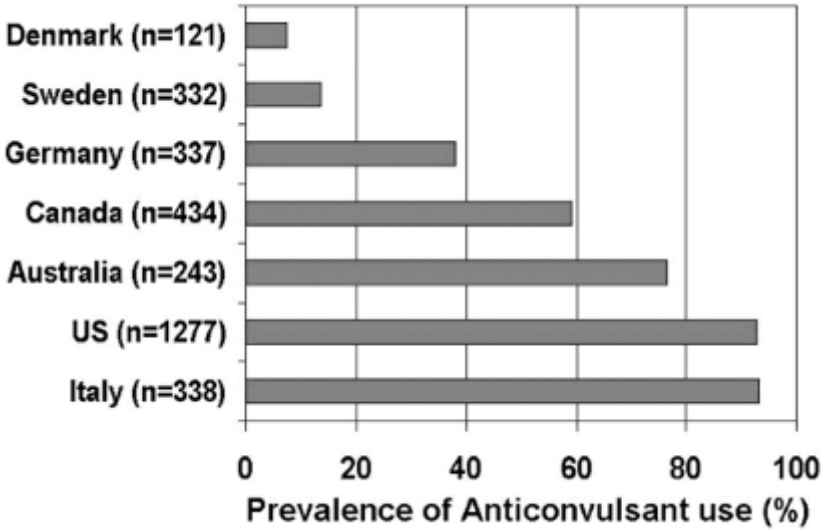


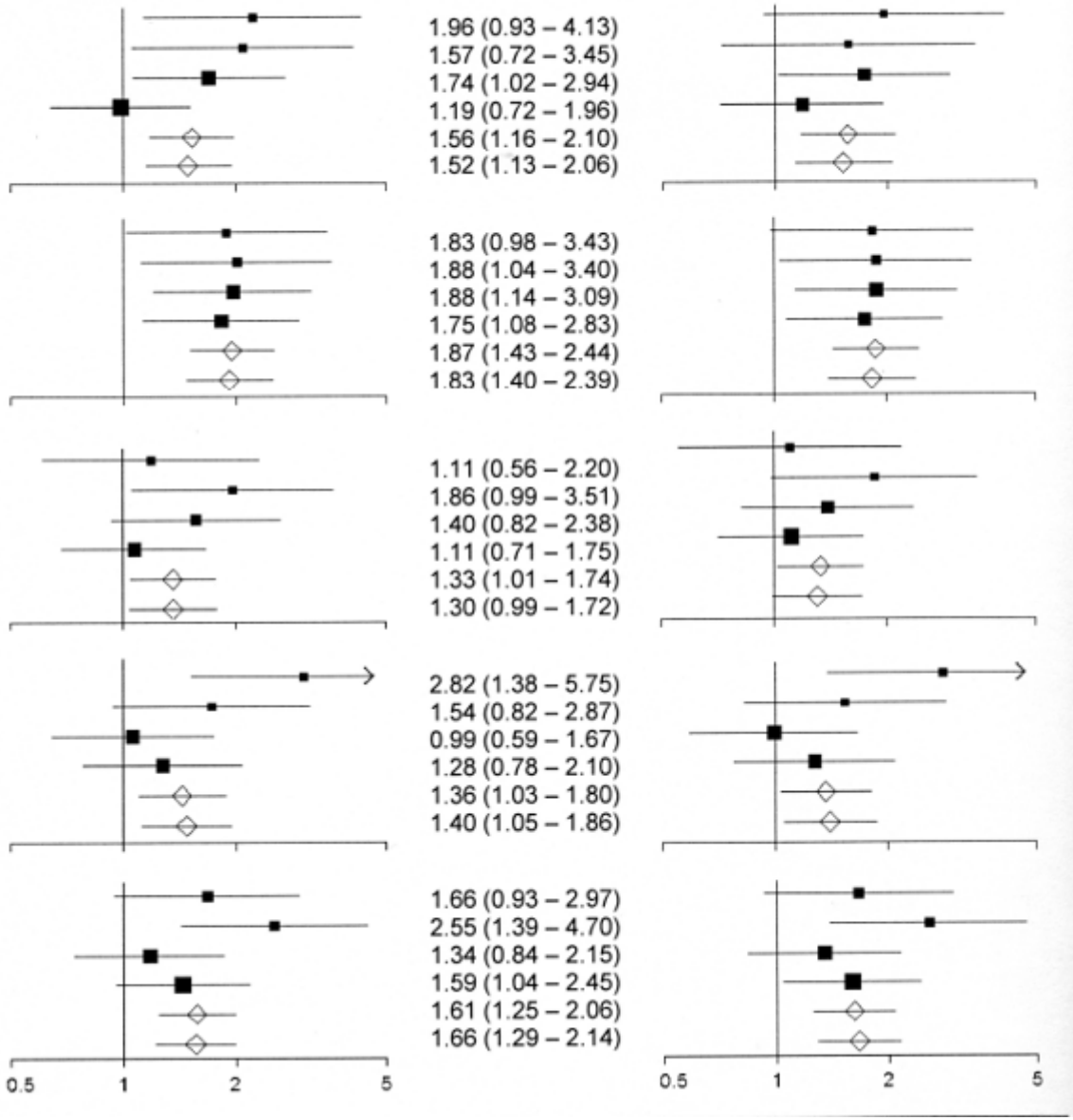
TABLE 1

Use of AEDs in 3552 patients with SAH

Drug Used	No. of Patients (%)
any AED	2313 (65.1)
phenytoin	1873 (52.7)
phenobarbital	663 (18.7)
carbamazepine	83 (2.3)
phenytoin only	1587 (44.7)
phenobarbital only	394 (11.1)
carbamazepine only	31 (0.9)
phenytoin & phenobarbital	249 (7.0)
phenytoin & carbamazepine	32 (0.9)
phenobarbital & carbamazepine	15 (0.4)
all three drugs	5 (0.1)

Mayor efecto detrimental en HSA difusa y sin HIP

Endpoints	OR adjusted for study center OR (95% CI)	OR adjusted for study center, neurological grade, age, SBP OR (95% CI)
Poor outcome (GOS)*		
Lanzino *et al.* 1999[14]	2.23 (1.14 – 4.33)	1.96 (0.93 – 4.13)
Haley *et al.* 1997	2.09 (1.06 – 4.12)	1.57 (0.72 – 3.45)
Lanzino *et al.* 1999[15]	1.70 (1.06 – 2.71)	1.74 (1.02 – 2.94)
Kassell *et al.* 1996	0.99 (0.64 – 1.52)	1.19 (0.72 – 1.96)
Pooled dataset	1.52 (1.18 – 1.98)	1.56 (1.16 – 2.10)
Meta-analysis	1.49 (1.15 – 1.95)	1.52 (1.13 – 2.06)
Symptomatic Vasospasm		
Lanzino et al. 1999[14]	1.89 (1.02 – 3.50)	1.83 (0.98 – 3.43)
Haley et al. 1997	2.01 (1.12 – 3.62)	1.88 (1.04 – 3.40)
Lanzino et al. 1999[15]	1.96 (1.20 – 3.19)	1.88 (1.14 – 3.09)
Kassell et al. 1996	1.83 (1.13 – 2.95)	1.75 (1.08 – 2.83)
Pooled dataset	1.94 (1.50 – 2.53)	1.87 (1.43 – 2.44)
Meta-analysis	1.92 (1.47 – 2.50)	1.83 (1.40 – 2.39)
Cerebral Infarction		
Lanzino *et al.* 1999[14]	1.19 (0.61 – 2.33)	1.11 (0.56 – 2.20)
Haley *et al.* 1997	1.97 (1.06 – 3.66)	1.86 (0.99 – 3.51)
Lanzino *et al.* 1999[15]	1.57 (0.93 – 2.65)	1.40 (0.82 – 2.38)
Kassell *et al.* 1996	1.07 (0.69 – 1.68)	1.11 (0.71 – 1.75)
Pooled dataset	1.36 (1.04 – 1.77)	1.33 (1.01 – 1.74)
Meta-analysis	1.36 (1.04 – 1.79)	1.30 (0.99 – 1.72)
High Temperature (day 8)		
Lanzino *et al.* 1999[14]	3.03 (1.52 – 6.04)	2.82 (1.38 – 5.75)
Haley *et al.* 1997	1.72 (0.94 – 3.16)	1.54 (0.82 – 2.87)
Lanzino *et al.* 1999[15]	1.06 (0.65 – 1.75)	0.99 (0.59 – 1.67)
Kassell *et al.* 1996	1.28 (0.78 – 2.08)	1.28 (0.78 – 2.10)
Pooled dataset	1.43 (1.09 – 1.88)	1.36 (1.03 – 1.80)
Meta-analysis	1.48 (1.12 – 1.95)	1.40 (1.05 – 1.86)
Neurological worsening**		
Lanzino *et al.* 1999[14]	1.68 (0.95 – 2.96)	1.66 (0.93 – 2.97)
Haley *et al.* 1997	2.53 (1.43 – 4.48)	2.55 (1.39 – 4.70)
Lanzino *et al.* 1999[15]	1.18 (0.74 – 1.87)	1.34 (0.84 – 2.15)
Kassell *et al.* 1996	1.44 (0.96 – 2.18)	1.59 (1.04 – 2.45)
Pooled dataset	1.57 (1.24 – 2.00)	1.61 (1.25 – 2.06)
Meta-analysis	1.56 (1.22 – 1.99)	1.66 (1.29 – 2.14)



Uso de DFH y Nimodipina

- **DFH: interacción con citocromo P450.**
- **Favorece el metabolismo de la *nimodipina y disminuye su biodisponibilidad***

- Estudio coadministración de nimodipina con inductores del cit P450 reduce en un 83 % el área bajo la curva de concentración tiempo (DFH y carbamacepina , no ocurre con valproico)

- BAYER: no recomienda coadministración con drogas inductoras

Tartara A, Galimberti CA, Manni R, Parietti L, Zucca C, Baasch H, Caresia L, Muck W, Barzaghi N, Gatti G. Differential effects of valproic acid and enzyme-inducing anticonvulsants on nimodipine pharmacokinetics in epileptic patients. *Br J Clin Pharmacol.* 1991;32:335–340.

Anticonvulsant Use and Outcomes After Intracerebral Hemorrhage

Andrew M. Naidech, Rajeev K. Garg, Storm Liebling, Kimberly Levasseur, Micheal P. Macken, Stephan U. Schuele and H. Hunt Batjer

Stroke published online Sep 24, 2009;

- Se enrolaron 98 pacientes
- (EEG con depresión del estado de conciencia): 59 % no recibió;
- *12 levetitacetan (12 %*), 22(22%) DFH y 6 (6%) ambos

Table 5. Logistic Regression Model for Nonindependence or Worse (mRS 4–6) at 3 Months*

Variable	OR (95% CI)	*P*
Admit NIHSS, per point	1.3 (1.1–1.5)	<0.001
Age, per year	1.08 (1.02–1.15)	0.02
PHT prophylaxis	9.0 (1.2–68.5)	0.03
ICH volume, per mL	1.001 (0.97–1.03)	0.9
Intraventricular hemorrhage	1.2 (0.2–6.7)	0.8
Infratentorial location	0.7 (0.02–17.4)	0.8

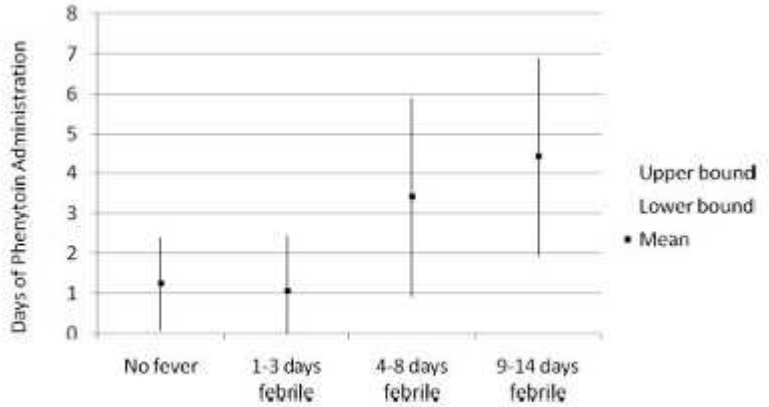


Figure. Longer duration of phenytoin use was associated with more febrile days (P=0.03). I-bars show mean and 95% CI.

•Levetiracetam no asoció a peor evolución

Bases para la utilizacion de Profilaxis.

- Prevenir convulsiones pues se asocian mal pronóstico
- Prevenir incremento de la PIC y deterioro neurológico con riesgo de aspiración
- Prevenir resangrado
- Prevenir desarrollo de epilepsia .
- EXISTE CONTROVERSIA ACERCA DE LA REAL UTILIDAD Y RELACIÓN COSTO BENEFICIO EN PACIENTES NEUROCRÍTICOS”

Prevenir el resangrado

- Las convulsiones se han relacionado con sangrado o resangrado no está claro si existe una relación de causalidad.
- En estudios que pudieron evaluar la temporalidad entre convulsiones y sangrado las mismas fueron consecuencia.
- Análisis multivariable: sólo el grado de H y H y el tamaño del aneurisma correlacionaron independientemente con riesgo de resangrado

Arch Neurol. 2005;62:410-416

neurocritical care society Neurocrit Care (2010) 12:165–172
DOI 10.1007/s12028-009-9304-y

ORIGINAL ARTICLE

Prospective, Randomized, Single-Blinded Comparative Trial of Intravenous Levetiracetam Versus Phenytoin for Seizure Prophylaxis

Jerzy P. Szaflarski · Kiranpal S. Sangha · Christopher J. Lindsell · Lori A. Shutter

Results A total of 52 patients were randomized (LEV = 34; PHT = 18); 89% with sTBI. When controlling for baseline severity, LEV patients experienced better long-term outcomes than those on PHT; the Disability Rating Scale score was lower at 3 months ($P = 0.042$) and the Glasgow Outcomes Scale score was higher at 6 months ($P = 0.039$). There were no differences between groups in seizure occurrence during cEEG (LEV 5/34 vs. PHT 3/18; $P = 1.0$) or at 6 months (LEV 1/20 vs. PHT 0/14; $P = 1.0$), mortality (LEV 14/34 vs. PHT 4/18; $P = 0.227$). There were no differences in side effects between groups (all $P > 0.15$) except for a lower frequency of worsened neurological status ($P = 0.024$), and gastrointestinal problems ($P = 0.043$) in LEV-treated patients.

Conclusions This study of LEV versus PHT for seizure prevention in the NSICU showed improved long-term outcomes of LEV-treated patients vis-à-vis PHT-treated patients. LEV appears to be an alternative to PHT for seizure prophylaxis in this setting.

AHA/ASA Guideline

Guidelines for the Early Management of Adults With Ischemic Stroke

A Guideline From the American Heart Association/ American Stroke Association Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups

The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists.

Prophylactic administration of anticonvulsants to patients with stroke but who have not had seizures is not recommended (Class III, Level of Evidence C).

(*Stroke.* 2007;38:1655-1711.

AHA/ASA Guideline

Guidelines for the Prevention of Stroke in Patients With Stroke or Transient Ischemic Attack

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

En ausencia de convulsiones el uso rutinario de drogas antiepilépticas no esta recomendado.
Case III. Nivel de evidencia C

Stroke. 2011;42:00-00.

EFNS guideline on the treatment of cerebral venous and sinus thrombosis in adult patients

K. Einhäupl[a], J. Stam[b], M. -G. Bousser[c], S. F. T. M. de Bruijn[d], J. M. Ferro[e], I. Martinelli[f] and F. Masuhr[a]

La profilaxis antiepiléptica puede ser una opción terapéutica en pacientes con déficit neurológico focal y lesiones supratentoriales en la admisión TAC /RM. La duración óptima del tratamiento no es clara

European Journal of Neurology 2010, **17:** 1229–1235

Seizures and Antiepileptic Drugs
Hemorragia Intracerebral

1. Clinical seizures should be treated with antiepileptic drugs *(Class I; Level of Evidence: A). (Revised from* the previous guideline)

Continuous EEG monitoring is probably indicated in ICH patients with depressed mental status out of proportion to the degree of brain injury (Class IIa; Level of Evidence: B).

Prophylactic anticonvulsant medication **should not be used *(Class III; Level of Evidence: B). (New recommendation)***

AHA GUIDELINES . July 2010

AHA/ASA Guideline

Guidelines for the Management of Spontaneous Intracerebral Hemorrhage

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists.

The American Association of Neurological Surgeons and the Congress of Neurological Surgeons have reviewed this document and affirm its educational content.

Prophylactic anticonvulsant medication should not be used *(Class III; Level of Evidence: B).*

(*Stroke*. 2010;41:2108-2129.

Recommendations for the Management of Intracranial Haemorrhage – Part I: Spontaneous Intracerebral Haemorrhage

The European Stroke Initiative Writing Committee and the
Writing Committee for the EUSI Executive Committee

Early prophylactic treatment of seizures is not recommended for all patients, but may be considered for selected patients with lobar ICH. In all other cases seizures should only be treated if they occur (level C). If seizures occur, a step-wise administration of antiepileptic drugs is generally recommended (table 4). Antiepileptic treatment should be continued for 30 days. After this time treatment should be reduced and eventually discontinued. If seizures reoccur, patients should receive chronic treatment with anticonvulsants.

Cerebrovasc Dis 2006;22:294–316

AHA/ASA Guideline

Guidelines for the Management of Aneurysmal Subarachnoid Hemorrhage

A Statement for Healthcare Professionals From a Special Writing Group of the Stroke Council, American Heart Association

The American Academy of Neurology affirms the value of this statement as an educational tool for neurologists.

The administration of prophylactic anticonvulsants may be considered in the immediate posthemorrhagic period **(Class IIb, Level of Evidence B)**.
The routine long-term use of anticonvulsants is not recommended **(Class III, Level of Evidence B)** but may be considered for patients with risk factors such as prior seizure, parenchymal hematoma, infarct, or middle cerebral artery aneurysms **(Class IIb, Level of Evidence B)**.

Stroke 2009, 40:994-1025

Critical Care Management of Patients Following Aneurysmal Subarachnoid Hemorrhage: Recommendations from the Neurocritical Care Society's Multidisciplinary Consensus Conference

Michael N. Diringer · Thomas P. Bleck · J. Claude Hemphill III · David Menon · Lori Shutter · Paul Vespa · Nicolas Bruder · E. Sander Connolly Jr. · Giuseppe Citerio · Daryl Gress · Daniel Hänggi · Brian L. Hoh · Giuseppe Lanzino · Peter Le Roux · Alejandro Rabinstein · Erich Schmutzhard · Nino Stocchetti · Jose I. Suarez · Miriam Treggiari · Ming-Yuan Tseng · Mervyn D. I. Vergouwen · Stefan Wolf · Gregory Zipfel

- Routine use of anticonvulsant prophylaxis with phenytoin is not recommended after SAH (low quality evidence—strong recommendation).
- Routine use of other anticonvulsants for prophylaxis may be considered (very low quality evidence—weak recommendation).
- If anticonvulsant prophylaxis is used, a short course (3–7 days) is recommended (low quality evidence—weak recommendation).

Neurocritical Care July 2011

Guidelines for the Management of Aneurysmal Subarachnoid Hemorrhage

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

The American Academy of Neurology affirms the value of this statement as an educational tool for neurologists.

Endorsed by the American Association of Neurological Surgeons and Congress of Neurological Surgeons; and by the Society of NeuroInterventional Surgery

E. Sander Connolly, Jr, MD, FAHA, Chair; Alejandro A. Rabinstein, MD, Vice Chair; J. Ricardo Carhuapoma, MD, FAHA; Colin P. Derdeyn, MD, FAHA; Jacques Dion, MD, FRCPC; Randall T. Higashida, MD, FAHA; Brian L. Hoh, MD, FAHA; Catherine J. Kirkness, PhD, RN; Andrew M. Naidech, MD, MSPH; Christopher S. Ogilvy, MD; Aman B. Patel, MD; B. Gregory Thompson, MD; Paul Vespa, MD, FAAN; on behalf of the American Heart Association Stroke Council, Council on Cardiovascular Radiology and Intervention, Council on Cardiovascular Nursing, Council on Cardiovascular Surgery and Anesthesia, and Council on Clinical Cardiology

(*Stroke*. 2012;43:1711-1737.)

Management of Seizures Associated With aSAH: Recommendations

1. **The use of prophylactic anticonvulsants may be considered in the immediate posthemorrhagic period *(Class IIb; Level of Evidence B).***
2. **The routine long-term use of anticonvulsants is not recommended *(Class III; Level of Evidence B)* but may be considered for patients with known risk factors for delayed seizure disorder, such as prior seizure, intracerebral hematoma, intractable hypertension, infarction, or aneurysm at the middle cerebral artery *(Class IIb; Level of Evidence B).***

JUNE 2012

Current Treatment Options in Neurology
DOI 10.1007/s11940-012-0180-y

EPILEPSY (E WATERHOUSE, SECTION EDITOR)

Seizure Treatment in Transplant Patients

Paul W. Shepard, BA
Erik K. St. Louis, MD[*]

Address
[*]Departments of Neurology and Medicine, Mayo Clinic and Foundation, 200 First Street Southwest, Rochester, MN 55905, USA
Email: stlouis.erik@mayo.edu

Keywords Transplant · Seizure · Epilepsy · Status epilepticus · Acute repetitive seizures · Posterior reversible encephalopathy syndrome · PRES · Infection · Antiepileptic drugs · Cyclosporine toxicity · Tacrolimus toxicity · Treatment

Opinion statement

Solid organ transplantation is frequently complicated by a spectrum of seizure types, including single partial-onset or generalized tonic-clonic seizures, acute repetitive seizures or status epilepticus, and sometimes the evolution of symptomatic epilepsy. There is currently no specific evidence involving the transplant patient population to guide the selection, administration, or duration of antiepileptic drug (AED) therapy, so familiarity with clinical AED pharmacology and application of sound judgment are necessary for successful patient outcomes. An initial detailed search for symptomatic seizure etiologies, including metabolic, infectious, cerebrovascular, and calcineurin inhibitor treatment-related neurotoxic complications such as posterior reversible encephalopathy syndrome (PRES), is imperative, as underlying central nervous system disorders may impose additional serious risks to cerebral or general health if not promptly detected and appropriately treated. The mainstay for post-transplant seizure management is AED therapy directed toward the suspected seizure type. Unfavorable drug interactions could place the transplanted organ at risk, so choosing an AED with limited interaction potential is also crucial. When the transplanted organ is dysfunctional or vulnerable to rejection, AEDs without substantial hepatic metabolism are favored in post-liver transplant patients, whereas after renal transplantation, AEDs with predominantly renal elimination may require dosage adjustment to prevent adverse effects. Levetiracetam, gabapentin, pregabalin, and lacosamide are drugs of choice for treatment of partial-onset seizures in post-transplant patients given their efficacy spectrum, generally excellent tolerability, and lack of drug interaction potential. Levetiracetam is the drug of choice for primary generalized seizures in post-transplant patients. When intravenous drugs are necessary for acute seizure management, benzodiazepines and fosphenytoin are the traditional and best evidence-based options, although intravenous levetiracetam, valproate, and lacosamide are emerging options. Availability of several newer AEDs has greatly expanded the therapeutic armamentarium for safe and efficacious treatment of post-transplant seizures, but future prospective clinical trials and pharmacokinetic studies within this specific patient population are needed.

Published online: 02 June 2012

TRASPLANTADOS

Levetiracetam is the drug of choice for primary generalized seizures in post-transplant patients.

TUMORES

neurocritical care society Neurocrit Care (2012) 16:109–113
DOI 10.1007/s12028-011-9626-4

ORIGINAL ARTICLE

Phenytoin, Levetiracetam, and Pregabalin in the Acute Management of Refractory Status Epilepticus in Patients with Brain Tumors

Christa B. Swisher · Meghana Doreswamy · Krista J. Gingrich · James J. Vredenburgh · Brad J. Kolls

Conclusion Our study suggests that the administration of PHT, LEV, and PGB in brain tumor patients with RSE is safe and highly effective.

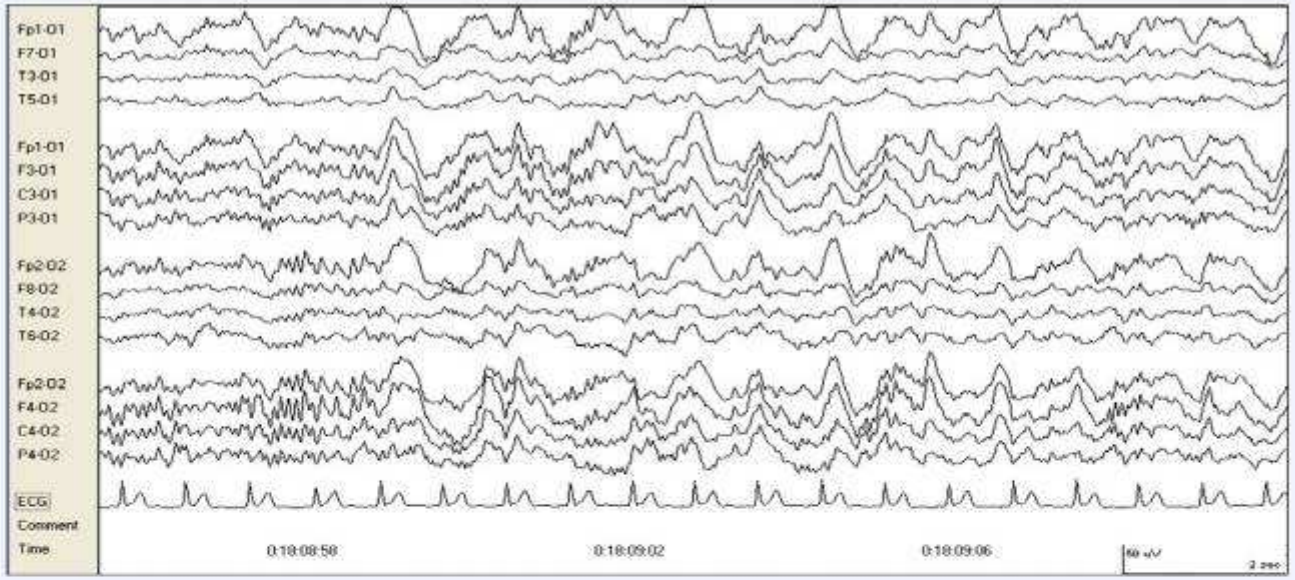
Epilepsy & Behavior
Volume 18, Issue 4, August 2010, Pages 491-493

Effect of music on the recovery of a patient with refractory nonconvulsive status epilepticus.

Kuester G, Rios L, Ortiz A, Miranda M.
Department of Neurology, Clinica Las Condes, Santiago. Chile; Center for Epilepsies, Clinica Las Condes, Santiago. Chile.

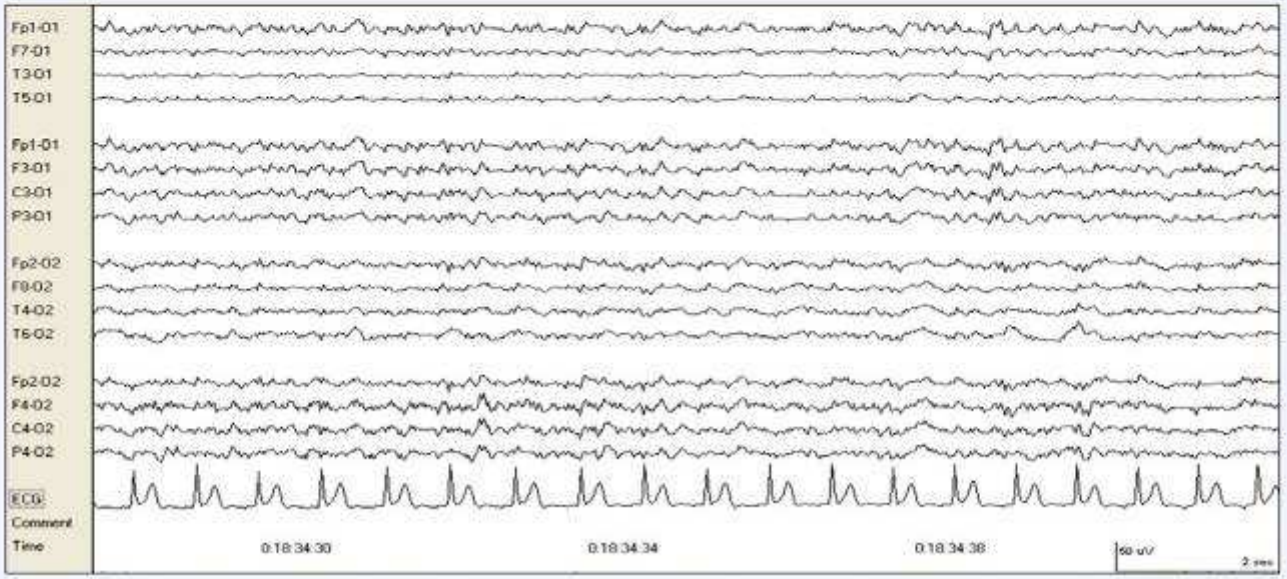
Abstract
The effect of music in epilepsy has been reported as beneficial but mainly in the interictal condition. There are no reports of the effect of music in an acute condition such as status epilepticus. Herein, we report a remarkable response to music in a patient with medically refractory nonconvulsive status epilepticus..

A



sonata for two pianos by Mozart K 448
30 minutes a day

B



The patient, a 22-year-old man, had severe brain trauma and was admitted to our clinic with a Coma Glasgow Scale score of 4. Surgery was performed to drain extracranial hematomas revealed by a CT scan. MRI showed multiple hemorrhagic contusions and diffuse axonal damage. He developed persistent impairment of consciousness secondary to nonconvulsive status epilepticus. He was treated unsuccessfully with midazolam 20 mg/hour, levetiracetam up to 4 g, then 3 g of valproic acid, following which hyperammonemia developed. Subsequently, topiramate, up to 800 mg, induced hepatitis and had to be withdrawn as well. Following 5 days of refractory status, informed written consent was obtained from the patient`s parents and he was exposed to music (***sonata for two pianos by Mozart K 448) for 30 minutes a day***. His EEG was monitored before and during his exposure to music. The EEG was evaluated in a blinded fashion at the time of musical intervention by two experienced neurophysiologists. The EEG changes are shown in Fig. 1. After 5 days of exposure to the music and improvement in epileptic discharges on the EEG, we instituted progressive withdrawal of anti-convulsants. The patient recovered from the coma and his cognitive and motor skills gradually improved; this improvement continued up to the last follow-up 4 months after his trauma. ***One hour daily of music was maintained as part of intense rehabilitation physiotherapy.***

ROBOTIC servira para evitar errores ?

GRACIAS !

europa y montreal 2011 277.MPG

Epilepsia, **48**(Suppl. 8):61–65, 2007
doi: 10.1111/j.1528-1167.2007.01353.x

CLINICAL ASPECTS OF STATUS EPILEPTICUS

The surgical treatment of status epilepticus

*Samden D. Lhatoo and †Andreas V. Alexopoulos

*Department of Neurology, Institute of Clinical Neurosciences, Frenchay Hospital, Bristol, United Kingdom; and †Cleveland Clinic Epilepsy Center, Neurological Institute, Cleveland, Ohio, U.S.A.

Table 1. Surgical procedures used in refractory status epilepticus

Focal resection
Lobar resection
Multilobar resection
Hemispherectomy—functional/anatomical/modified
Corpus callosotomy
Multiple subpial transaction ± focal resection
Vagal nerve stimulator implantation
Low-frequency repetitive cortical electrical stimulation

THE IDEAL SURGICAL CANDIDATE WITH STATUS EPILEPTICUS

Patients with convulsive or nonconvulsive RSE who have a high degree of concordance between semiology, imaging, functional imaging with PET or SPECT and EEG (scalp as well as invasive) indicating a single epileptogenic zone, with focal cortical dysplasia as the underlying pathology, appear most likely to benefit. However, the optimal timing for surgery is unclear. Substantial morbidity and mortality are likely to accrue with increasing duration of RSE. Some have suggested a two week period of failed medical treatment as sufficient justification for surgery.

neurocritical care society Neurocrit Care (2007) 7:86–91
DOI 10.1007/s12028-007-0038-4

PRACTICAL PEARL

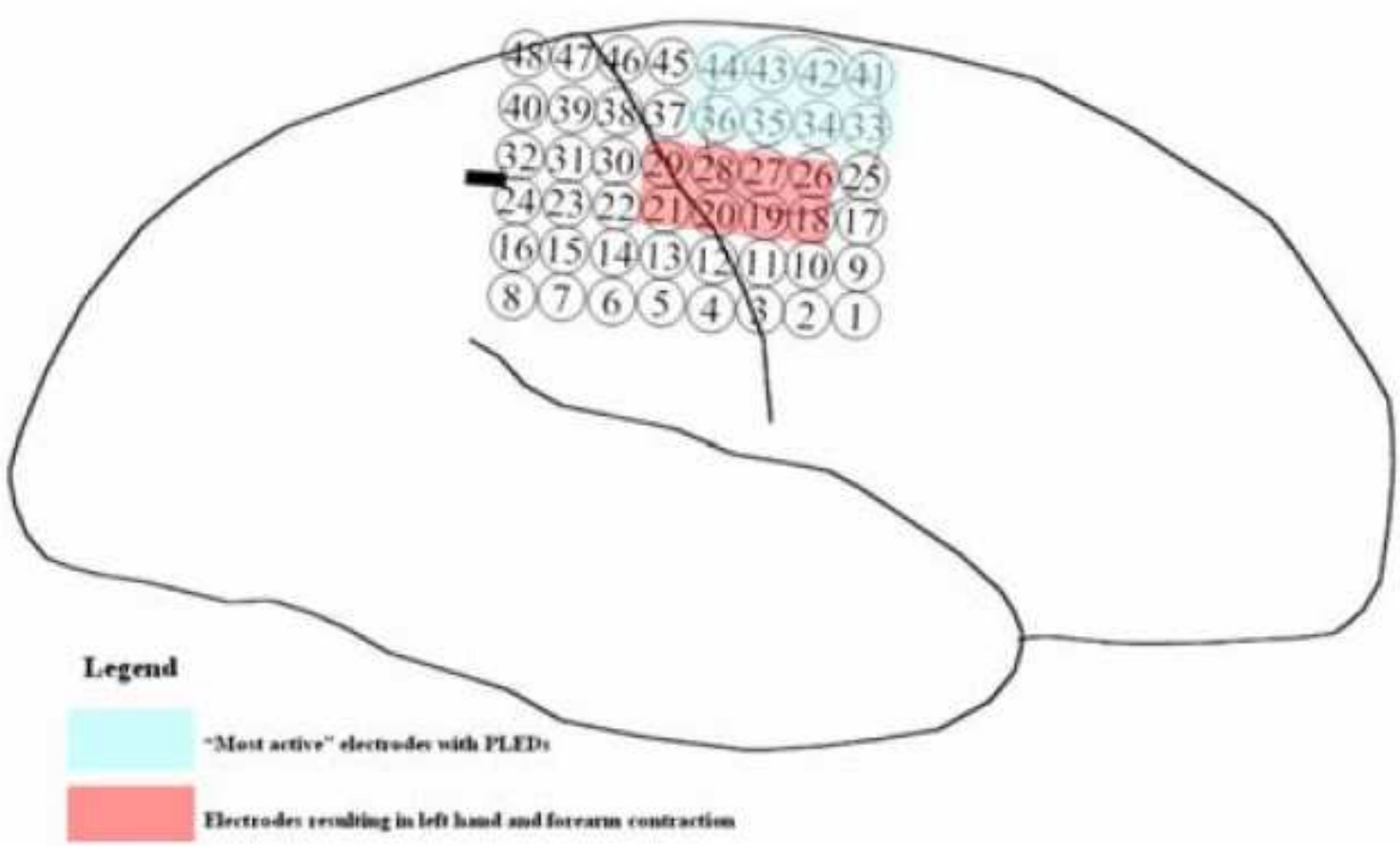
The role of neurosurgery in status epilepticus

Yu-tze Ng · Ruth E. Bristol · Dewi V. Schrader · Kris A. Smith

Table 1 Summary of previously published neurosurgery performed for different forms and etiologies of status epilepticus

Number of cases	Age(s)	Diagnosis	Seizure type	Surgical procedure	Author
7	5 mo-6.5 yrs	Hemimegencephaly Encephalomalacia, RE, HD	FMSE CPSE IS	Hemi-spherectomy	Alexopoulos et al. [22] Duane et al. [10]
8	2 mo–31 yrs	FCD (lesional on MRI), Tuberous sclerosis - Multiple tubers	CPSE FMSE Tonic	Focal (cortical) resection	Alexopoulos et al. [22] Ng et al. [9] Ng et al. [11] Xa et al. [20] Gorman et al. [27] Krsek et al. [28]
8	3 mo–36 yrs	Non-lesional MRI scan ± FCD (pathology)	FMSE EPC CPSE	Focal (cortical) resection MSTs	Desbiens et al. [25] Ng et al. [10] Costello et al. [26] D'Giano et al. [14] Xa et al. [23]
2	19 yrs, 29 yrs	FCD Non-lesional	EPC NCSE	Isolated MSTs	Molyneux et al. [13] Bristol et al. [15]
1	30 mo	Hypothalamic hamartoma	Status gelasticus	Transcallosal, endoscopic resection	Ng et al. [9, 12]
1	25 yrs	Non-lesional	GCSE	Corpus callosotomy	Xa et al. [23]
1	2 yrs	Cavernous malformation	EPC	Lesionectomy	Ng et al. [9]
2	13 yrs, 30 yrs	Non-lesional	CPSE GCSE	VNS	Winston et al. [29] Patwardhan et al. [30]

FMSE, focal motor status epilepticus; CPSE, complex partial status epilepticus; RE, Rasmussen encephalitis; HD, hemicortical dysplasia; IS, infantile spasms, FCD, focal cortical dysplasia; EPC, epilepsia partialis continua; MSTs, multiple subpial transections; NCSE, non-convulsive status epilepticus; GCSE, generalized convulsive status epilepticus; VNS, vagus nerve stimulation



Schematic diagram of where the subdural grid was placed. The maximal seizure activity was seen over the superior, anterior quadrant (overlying most of the tumor, shown by circle) and the only motor area found was in the center of the grid, with left forearm and hand flexion

Neurol Med Chir (Tokyo) 46, 240 ~ 243, 2006

Transient Occipitotemporal Subcortical Diffusion-Weighted Magnetic Resonance Imaging Abnormalities Associated With Status Epilepticus

—Case Report—

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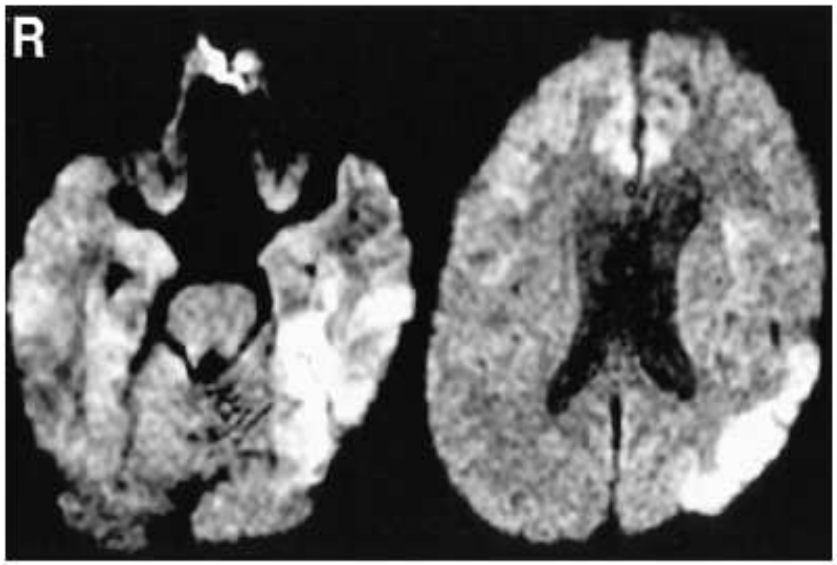
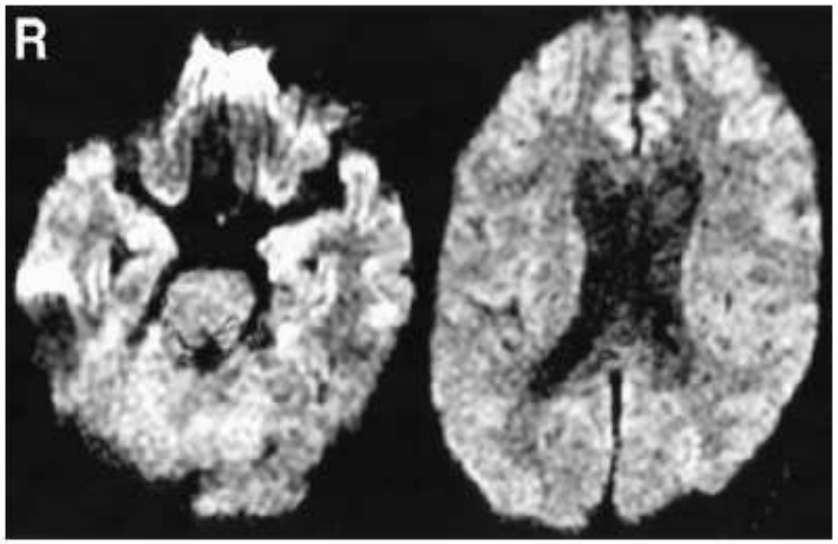
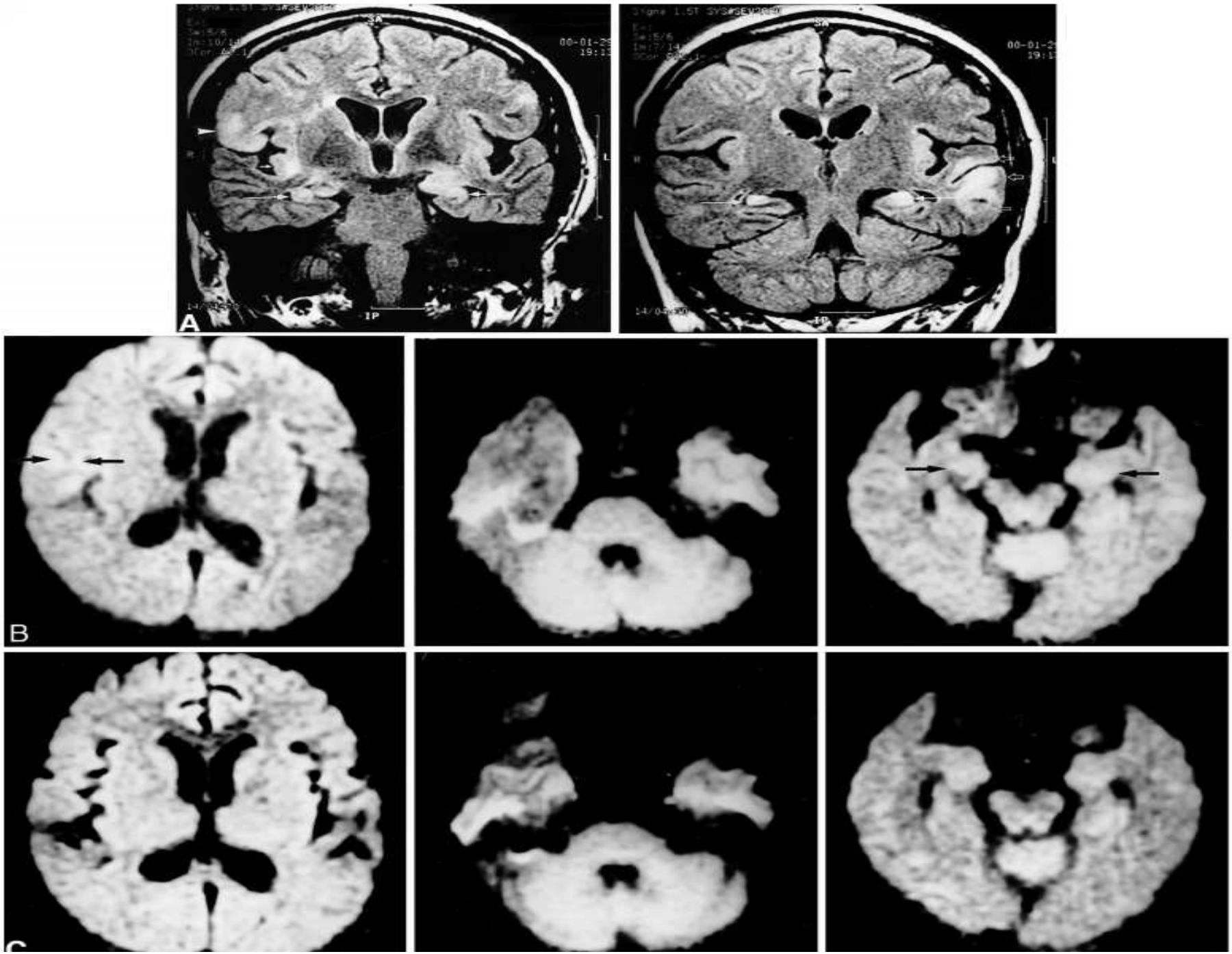


Diffusion-weighted magnetic resonance images on admission demonstrating high intensity areas in the left temporal and occipital lobes.



Diffusion-weighted magnetic resonance images performed 1 month after admission revealing nearly complete disappearance of the high intensity areas.


A
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AJNR Am J Neuroradiol 22:1149–1160, June/July 2001

Transient MR Signal Changes in Patients with Generalized Tonicoclonic Seizure or Status Epilepticus: Periictal Diffusion-weighted Imaging

Jeong-Ah Kim, Jin Il Chung, Pyeong Ho Yoon, Dong Ik Kim, Tae-Sub Chung, Eun-Ju Kim, and Eun-Kee Jeong

CONCLUSION: The MR signal changes that occur after generalized tonicoclonic seizure or status epilepticus are transient increase of signal intensity and swelling at the cortical gray matter, subcortical white matter, or hippocampus on periictal T2-weighted and diffusion-weighted images. These findings reflect transient cytotoxic and vasogenic edema induced by seizure. The reversibility and typical location of lesions can help exclude the epileptogenic structural lesions.

TABLE 2: Periictal MR signal changes and single-photon emission CT findings

Patient	Initial MR					Location of MR Signal Change	Location of Increased Perfusion of SPECT
	T2	T1	CE	DWI	FLAIR		
1	+	−	−			Bilateral cingulate gyri	Bilateral superior frontoparietal
2	+	−	−	↑	+	Bilateral cuneus, precuneus	Bilateral parietooccipital
3	+	+	−			Left parietal	
4	+	+	↑			Left frontoparietal	Left frontotemporoparietal
5	+	+	↑↑	↑↑	+	Right parahippocampal, Right uncal, Right occipital	Right temporal, Right parahippocampal
6	+	+	−	↑↑	+	Right hippocampus	
7	+	+	↑	↑↑	+	Left temporal, hippocampal, uncus	Left temporal, Left insular
8	+	+	↑↑	↑↑	+	Bilateral frontotemporal, hippocampal	Bilateral temporal, parietooccipital

Note.—CE, contrast enhancement; DWI, diffusion-weighted image; FLAIR, fluid attenuated inversion recovery; T1, T1-weighted image; T2, T2-weighted image; +, visible signal change; −, no visible signal change; ↑, mild degree of increased signal intensity; ↑↑, high degree of increased signal intensity.