Guidelines to be followed by centres, services and units in order to be designated as Reference Centres, Services and Units of the National Health System, as agreed by the Interterritorial Board

39. REFRACTORY EPIPLEPSY

Epilepsy refractory to pharmacological treatment is the properly diagnosed epilepsy which has an unsatisfactory control of the seizures (having an impact in the patient's quality of life) with the use of anti-epileptic drugs (AEDs), in monotherapy as well as in those reasonably possible combinations, in maximum doses not causing incapacitating side effects, and during enough time in order to ensure their ineffectiveness. Around 30% of the patients with epilepsy are estimated to be refractory to pharmacological treatment.

The main characteristics of refractory epilepsy may be summarized as follows:
-Unsatisfactory control of the seizures: AEDs are not successful in decreasing the frequency and/or severity of the seizures, according to patient's quality of life criteria (which will depend on the frequency, type, time of occurrence and consequences of the seizures, as well as other professional, social and psychological factors).
-Existence of incapacitating side effects of the AEDs: In general these are neurotoxic side effects dependent on the dosage.
-Persistence of the epileptic seizure despite the treatment with AEDs: The AEDs used must be optimal for the type of epilepsy, they must be administered in maximum tolerated doses, treatment duration must be long enough and will depend on the seizure baseline rate.

An *epilepsy unit* is defined as the unit providing diagnostic and therapeutic service, including surgery, to patients with epilepsy. It must be formed by neurologists, neurophysiologists and neurosurgeons; in collaboration with specialist from other areas such as neuroradiolgy, psychiatry, clinical psychology, anaesthesia; as well as nursing staff with training and experience in the field. Diagnostic and therapeutic ability of the highly specialized epilepsy unit is described in a document from the American Electroencephalographic Society.

Furthermore, according to different studies, at least 20% of the patients with refractory epilepsy are estimated to suffer non epileptic psychogenic seizures; only units with experience may provide the diagnosis through a prolonged video-EEG monitoring.

A. Rationale for the proposal

► Epidemiological data on epilepsy (incidence and prevalence).	Epilepsy is the most common chronic neurological disorder. Incidence of epilepsy varies in terms of age and fluctuates between 30-230 per every 100,000 people and year, according to a European study. Out of these, 30% is diagnosed with refractory epilepsy. Incidence of refractory epilepsy is 6/100,000; In Spain, there could be an incidence of 2,400 patients/year, approximately 50% with generalized epilepsy and 50% with focal. Epilepsy prevalence is 4-8/1,000 population; therefore, in Spain there would be around 200,000 patients with epilepsy; out of these, approximately 60,000 with refractory epilepsy.
► Data on the use of surgery for epilepsy.	- Out of all the patients with refractory epilepsy assessed for epilepsy surgery, a variable percentage fluctuating between 10-20% are candidates to the surgery, depending on the selection criteria. - Epilepsy surgery, also depending on its complexity, has a success rate fluctuating between 30-85%.

B. Guidelines to be followed by Centres, Services and Units in order to be designated as Reference Centres, Services and Units for the care of refractory epilepsy:

► Experience of the Reference Centres, Services and Units: - Activity: • Number of refractory epilepsy surgeries that should be performed in a year to ensure an adequate care.	- 15-20 refractory epilepsy surgeries in a year.

- Other data: research on the subject, postgraduate teaching, continuing training, publications, etc.	- Accredited postgraduate teaching: Unit participation in the internship and residency programme of the Centre. - Participation in research projects and publications in the field[a]. - Continuing training programme standardized and authorized by the centre's board of directors. - Clinical multidisciplinary sessions, at least once a month, in order to make decisions and coordinate treatments.
► Specific resources of the Reference Centres, Services and Units:	
- Human resources required for the adequate care of refractory epilepsy.	Multidisciplinary care provided by: - 2 neurologists. - 2 neurophysiologists. - 2 neurosurgeons. - 24 hour continuous neurologic and neurosurgical care, given the need for postoperative monitoring. - 24 hour programmed care of neurophysiology, given the need for prolonged video-EEG recording during days. - Nursing and surgical staff.
- Basic education of the team members[b].	- Specialists with 3 year experience in diagnosis and medico-surgical treatment of refractory epilepsy, both for paediatric age and adults. - Nursing staff with experience in neurology, neurosurgery and video-EEG as well as assisting and treating epileptic patients.
- Specific equipment required for the adequate care of refractory epilepsy.	- Hospitalization unit, with at least 2 beds ensuring 24 hours EEG monitoring of admitted patients as well as supervision (24 hours a day) by qualified staff. - Neurophysiological equipment: Equipment for prolonged video-EEG recording with, at least, 64 recording

	channels. Cortical mapping equipment with deep stimulation electrodes both intra and extraoperative. Electrocorticography. - Neuropsychological equipment: Neuropsychological test battery equipment for brain dysfunction assessment. - Surgical equipment: Standard and microsurgical instruments for epilepsy surgery. Surgical instruments for subpial resection Neuronavigation system for controlled resection of brain and precise deep electrodes insertion. Equipment and instruments for insertion of invasive intracranial electrodes (cortical, intracranial and foramen ovale) for video-EEG recording. Instruments for intraoperative electrocorticography and brain mapping. Equipment for vagus nerve stimulator implantation and adjustment.
► Resources from other units and services besides those belonging to the Reference Centres, Services and Units required for the adequate care of refractory epilepsy [b].	- Diagnostic imaging services/unit with neuroimaging techniques and: ◆ CT scan. ◆ Brain angiogram. ◆ High resolution MRI, with the appropriate sequences for detection of mesial temporal sclerosis or other epileptogenic cortical injuries; it should allow performing functional MRI for testing language function and activation of eloquent brain areas. - Nuclear medicine services/unit, with experience in epileptic patients. - Psychiatry services/unit, with experience in epileptic patients. - Clinical psychology services/unit, with experience in epileptic patients. - Pharmacy services/unit, including 24 hours continuous service of anti-epileptic drugs. - Rehabilitation services/unit, with experience in epileptic patients. - Anaesthesia services/unit with experience in epileptic patients. - Intensive care services/unit, with experience in epileptic patients.

	- Social workers services/unit.
► Procedure and clinical results indicators of the Reference Centres, Services and Units [c]:	**The indicators will be agreed with the Units that will be designated.**
► Existence of an adequate IT system (Type of data that the IT system must include to allow identification of the activity and evaluation of the quality of the services provided)	- Filling up the complete MBDS of hospital discharge. - The unit must have a *registry of patients with refractory epilepsy* which at least must include: - Medical record number. - Date of birth. - Sex. - Patient's habitual region of residence. - Admission date and discharge date. - Type of admission (Emergency, planned, other). - Type of discharge (Home, hospital transfer, voluntary, death, transfer to a healthcare centre, other.) - Service in charge of patient's discharge. - Main diagnosis (ICD-9-CM). - Other diagnosis (ICD-9-CM). - Diagnostic procedures provided to the patient (ICD-9-CM): Type of procedure and date when it was provided. - Therapeutic procedures provided to the patient (ICD-9-CM): Type of procedure and date when it was provided. ◆ Number and type of surgical procedures performed in relation to refractory epilepsy surgery. ◆ Other therapeutic procedures. - Complications (ICD-9-CM). - Patient monitoring: Engel's Seizure Outcome Scale, 3, 6, and 12 months after and yearly.

	Other. - The unit must have the required data which should be sent to the Spanish National Health Service Reference Centres, Services and Units Appointment Commission Secretariat for yearly reference unit monitoring.

[a] *Criteria to be assessed by the Appointment Commission.*
[b] *Experience will be accredited by certification from the hospital manager.*
[c] *Clinical results standards, agreed to by the experts group, will be assessed, initially by the Appointment Commission, while in the qualification process, as more information from the Reference Centres, Services and Units is being obtained. Once qualified by the Appointment Commission, the Quality Agency will authorize its compliance, as for the rest of guidelines.*

Bibliography:

1. Kwan P, Brodie MJ. Early identification of refractory epilepsia. N Eng J Med 2000;342:314-9.
2. National Association of Epilepsy Centers. Guideline for Essential Services, Personnel, and Facilities in Specialized Epilepsy Centers in the United States. Epilepsia 2001;42:804-814.
3. Guideline twelve: guidelines for long-term monitoring for epilepsy. American Electroencephalographic Society. J Clin Neurophysiol 2008;25:170-180.
4. Walczak TS, Papacostas S, Williams DT, et al. Outcome after diagnosis of psychogenic non-epileptic seizures. Epilepsia 1995;36:1131-7.
5. French J, Estok R, Chopra S, et al. Improving research in patients with newly diagnosed epilepsy: recommendations from a systematic review of the literature. Neurology.
6. Juul-Jensen P, Foldspang A. Natural history of epileptic seizures. Epilepsia, 1986;24:297-312.
7. Hauser WA. The natural History of Seizures. In: Wylie E, ed. The treatment of epilepsy: Principles and practice. Philadelphia: Lea and Febiger; 1993:165-170.
8. Hauser WA, Hersdorffer DC. Epidemiology of intractable epilepsy. In: Lüders HO and Comair YG. Epilepsy Surgey. Philadelphia. Lippincot Williams and Wilkins; 2001:55-61.