

Definition of drug resistant epilepsy

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The ILAE has, for the first time, proposed a consensus definition of drug resistant epilepsy. An ad hoc task force was appointed under the Commission on Therapeutic Strategies in January 2008. The task force comprised members with diverse expertise, including epidemiology, adult and pediatric epileptology, neurosurgery, clinical pharmacology, and clinical trial design (Appendix). A series of formal and informal meetings, teleconferences and email exchanges took place during which pertinent literature was reviewed and controversial issues extensively discussed and debated. A draft report was circulated to all ILAE Commissions for comments in March 2009 and a final report was submitted to the Executive Committee in April 2009. The report was formally approved by the Executive Committee during the ILAE's Centenary Congress in Budapest, Hungary, June 28th to July 2nd, 2009, and after peer review, has been published in *Epilepsia* (ref.). It is also posted on the ILAE's Web site (www.ilae.org).

The ILAE task force has chosen the preferred term “drug resistant” to replace the terms medically intractable, refractory, and pharmaco-resistant. We feel this term is more consistent with the intent of the definition, namely to identify patients for whom there is sufficient information to predict that they will have a substantially poorer prognosis for seizure remission with AEDs when compared with the population as a whole.

“Intractable” and “refractory” would imply that there is no chance at all of remission, which is never the case.

This report will be an important addition to the family of ILAE classifications and terminologies. For a number of reasons, the definition of drug resistant epilepsy has been

controversial. Without consensus, diverse criteria or even a lack of explicit criteria have been employed by different clinicians and researchers, leading to an inability to compare findings across studies meaningfully or to craft practice recommendations. Thus a consensus definition may find application in broad scenarios, including (a) recommendations on when to refer patients to specialist centers for comprehensive review of diagnosis and management; (b) timing of consideration for alternative treatment modalities such as surgery; (c) selection of patients for clinical research studies of novel interventions; (d) clinical and basic research into the biology of drug resistance; (e) determination of the epidemiology of drug resistant epilepsy for planning of healthcare resources; (f) recognition of treatment resistant individuals for educational and welfare needs and other social purposes.

In attempting to address the particularly controversial elements, the proposed definition has several unique features. First, it stipulates the information required to assess the outcome of an intervention (such as an AED) so that different interventions can be measured with the same yardstick. Second, it provides guidance for the duration of seizure freedom required to define treatment success which is particularly relevant for individuals with infrequent seizures. Specifically, treatment success can only be determined after the individual has remained without seizures for either 3 times the prior inter-seizure interval or 1 year, whichever is longer. Third, the definition has two “hierarchical” levels. Level 1 is a scheme to categorize or characterize the outcome of an intervention (such as an AED), providing a framework to define treatment success or failure, based on which criteria for defining drug resistance are derived (level 2).

In essence, it is proposed that drug resistant epilepsy may be defined as *failure of adequate trials of two tolerated and appropriately chosen and used AED schedules (whether as monotherapies or in combination) to achieve sustained seizure freedom*. It is important to note that no seizure frequency requirement is necessary to meet the definition. Thus, an individual with one seizure per year can be regarded as treatment resistant. Given the paucity of high quality data, the proposed definition should not be regarded as a *fait accompli* but a common starting point for work in progress. We ask the clinical and research community to apply and test the definition in diverse settings so that it can be refined as new evidence emerges. Your feedback is crucial!

Reference:

Kwan P, Arzimanoglou A, Berg AT, Brodie MJ, Hauser WA, Mathern G, Moshé SL, Perucca E, Wiebe S, French J. Definition of drug resistant epilepsy. Consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies. *Epilepsia*. DOI: 10.1111/j.1528-1167.2009.02397.x

Appendix

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