

Antiepileptic Drug Withdrawal

Most [seizure recurrences](#) develop during the first 6 months after [Antiepileptic Drug withdrawal](#).

No consistent set of predictors could be identified because a large number of variables have been identified in the literature, many studies reported contradicting results, study populations varied considerably, and the quality of the original studies was often low. Meta-analysis of individual participant data is necessary, because it allows for (1) correction for differences in follow-up duration between subjects and studies, (2) a study of interaction effects, (3) calculation of more accurate estimates valid across several populations, and (4) the assessment of each predictor's effect size ¹⁾.

Seizure-free epilepsy patients on AED monotherapy who taper their medication may improve neuropsychological performance with a relative risk of seizure relapse of 2.46, compared to those continuing therapy ²⁾.

Indications for AED withdrawal

There is no [agreement](#) on how long a [patient](#) should be seizure-free before withdrawal of [anticonvulsants](#), nor is there agreement on the prognostic value of [EEGs](#) and on the best time period over which to withdraw AEDs.

The following is based on a study of 92 patients with idiopathic epilepsy, who had been free of seizures for two years ³⁾

Generalization, e.g. to [posttraumatic seizures](#), may not be appropriate. Taper was by 1 "unit" q 2 weeks (where a unit is defined as 200mg for [carbamazepine](#) or [valproic acid](#), or 100mg for [phenytoin](#)). Follow-up: mean = 26 mos (range: 6-62).

31 patients (34%) relapsed, with the average time to relapse being 8 mos (range: 1-36). Using actuarial methods, the risk for recurrence is 5.9%/month for 3 months, then 2.7%/month for 3 months, then 0.5%/month for 3 months. Factors found to affect the likelihood of relapse include:

1. [seizure](#) type: 37% relapse rate for generalized seizures; 16% for complex or simple partial; 54% for complex partial with secondary generalization
2. number of seizures before control attained: those with ≥ 100 seizures before control had statistically significant higher relapse rate than those with < 100
3. the number of drugs that had to be tried before single drug therapy successfully controlled seizures: 29% if 1st drug worked, 40% if a change to a 2nd drug was needed, and 80% if a change to a 3rd drug was required
4. [Engel Epilepsy Surgery Outcome Scale](#) : class 4 had worst prognosis for relapse. Epileptiform discharges on EEG serves to discourage AED withdrawal ⁴⁾

In a larger randomized study ⁵⁾, the most important factors identified to predict freedom from

recurrent seizures were:

1. longer seizure-free period
2. use of only one AED (vs. multiple AEDs)
3. seizures other than [tonic-clonic seizures](#).

Case series

The aim of this study was to determine the outcome of antiepileptic drug (AED) withdrawal in patients who were seizure-free for more than two years.

Methods: Patients with epilepsy who were seizure-free for at least two years and decided to stop AED therapy gradually were followed up every two months for seizure relapse. The inclusion criteria were as follows: (1) diagnosis of epilepsy, defined as the following conditions: ① at least two unprovoked (or reflex) seizures occurring >24 h apart; ② one unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years; ③ diagnosis of an epilepsy syndrome; (2) patients remained seizure-free for at least 24 consecutive months during AED therapy; and (3) patients expressed a desire to discontinue AED therapy gradually and agreed to return for regular follow-ups. The time to a seizure relapse and predictive factors were analyzed by survival methods, including sex; age at seizure onset; number of episodes; seizure-free period before AED withdrawal; duration of follow-up after AED withdrawal; AED tapering off period (taper period); results from brain magnetic resonance (MRI); electroencephalogram (EEG) after drug withdrawal; EEG before drug withdrawal; seizure type (classified as generalized, partial, or multiple types based on history); and the number of AEDs administered for long-term seizure control. A log-rank test was used for univariate analysis, and a Cox proportional hazard model was used for multivariate analysis.

Results: We selected 94 patients (58 men, 36 women). The relapse ratio was 29.8%. Univariate analysis and multivariate Cox regression analysis indicated that withdrawal times and multiple AEDs, as well as the seizure-free period before withdrawal and abnormal EEG after drug withdrawal were significantly correlated with seizure recurrence and were significant independent predictive factors, with a hazard ratio of 0.839 and 3.971, 0.957, and 3.684, respectively.

Significance: The relapse rate in our study was similar to commonly reported overall rates for epilepsy. Distinguishing variables, such as withdrawal times, multiple AEDs, seizure-free period before withdrawal, and abnormal EEG after drug withdrawal, need to be considered when choosing to withdraw from AEDs. Therefore, our recommendation is that after two years of seizure-free survival, patients could consider withdrawal unless they have hippocampal sclerosis (HS) ⁶⁾.

¹⁾

Lamberink HJ, Otte WM, Geleijns K, Braun KP. Antiepileptic drug withdrawal in medically and surgically treated patients: a meta-analysis of seizure recurrence and systematic review of its predictors. *Epileptic Disord.* 2015 Sep;17(3):211-28. doi: 10.1684/epd.2015.0764. PMID: 26292909.

²⁾

Lossius MI, Hessen E, Mowinckel P, Stavem K, Erikssen J, Gulbrandsen P, Gjerstad L. Consequences of antiepileptic drug withdrawal: a randomized, double-blind study (Akershus Study). *Epilepsia.* 2008 Mar;49(3):455-63. doi: 10.1111/j.1528-1167.2007.01323.x. Epub 2007 Sep 19. PMID: 17888074.

³⁾

Callaghan N, Garrett A, Goggin T. Withdrawal of Anticonvulsant Drugs in Patients Free of Seizures for

Two Years. N Engl J Med. 1988; 318:942-946

⁴⁾

Anderson T, Braathen G, Persson A, et al. A Comparison Between One and Three Years of Treatment in Uncomplicated Childhood Epilepsy: A Prospective Study. II. The EEG as Predictor of Outcome After Withdrawal of Treatment. Epilepsia. 1997; 38:225-232

⁵⁾

Medical Research Council Antiepileptic Drug Withdrawal Study Group. Randomized study of antiepileptic drug withdrawal in patients in remission. Lancet. 1991; 337:1175-1180

⁶⁾

Li Y, Chen S, Qin J, She Y, Chen Y, Liu X, Yu H, Zhou L. Risk of seizure recurrence from antiepileptic drug withdrawal among seizure-free patients for more than two years. Epilepsy Behav. 2020 Dec;113:107485. doi: 10.1016/j.yebeh.2020.107485. Epub 2020 Nov 3. PMID: 33157416.

From:

<https://neurosurgerywiki.com/wiki/> - **Neurosurgery Wiki**

Permanent link:

https://neurosurgerywiki.com/wiki/doku.php?id=antiepileptic_drug_withdrawal

Last update: **2025/04/29 20:28**

