

WHEN ARE SEIZURES CONSIDERED DRUG RESISTANT?



Has your child failed two anti-epileptic drugs?

Drug-resistant epilepsy is defined as *failure of adequate trials of two tolerated, appropriately chosen and used anti-epileptic drug schedules (whether as monotherapies or in combination) to achieve sustained seizure freedom.*

It is very important to understand the key phrases in this definition: adequate trials, tolerated, appropriately chosen, and sustained seizure freedom.

"Adequate trials"

This means that the drug was incrementally increased (titrated) to its effective dose range. If the drug was stopped due to adverse side effects (such as skin rash, for example) then it does not count as one of the two drugs in the definition. Unfortunately, it is difficult to rigidly define what is the effective dose range for each drug. This is why it's important that your child is seen by an experienced pediatric neurologist or, preferably, epileptologist who understands effective dose ranges for each drug. When your child is prescribed an anti-epileptic drug, ask the epileptologist when you should expect to see seizure control.

"Tolerated"

This means there are no noxious or unintended effects from using the drug. In other words, the drug chosen by the neurologist or epileptologist was tolerated by the child. All anti-epileptic drugs have some sort of side effect. Many of those side effects, such as sedation, confusion, or loss of appetite, are generally tolerated by most children. Behavioral side effects like aggression or agitation may be tolerated by one child, but may be so disruptive to everyday living in another child, then the drug must be stopped. Some anti-epileptic drugs, however, including phenytoin, valproate, and carbamazepine, can cause liver toxicity or liver failure. Others can cause very serious skin reactions such as Stevens Johnson syndrome and toxic epidermal necrolysis which can be fatal if untreated.

"Appropriately chosen"

The two drugs chosen by the neurologist or epileptologist must be appropriate for the type of epilepsy and seizure type. This means that the drug must have previously been shown to be effective for the seizure type. As an example, ethosuximide is not an appropriate drug for focal seizures and would not count toward the drug-resistant definition.

This is especially important in the case of infantile spasms, a particularly catastrophic type of seizure if unabated. The gold standard drugs for first-line therapy to stop infantile spasms include very high-dose corticosteroids such as prednisone and prednisolone, high dose adrenocorticotrophic hormone (known as ACTH), and vigabatrin (known as Sabril). If a child, for example, is given phenobarbital and Keppra to stop infantile spasms, they are not considered drug resistant because those are not first-line drugs for infantile spasms. It is imperative that a child with infantile spasms be seen by a neurologist or epileptologist with substantial experience treating infantile spasms so that the right drugs are given to the child immediately.

"Sustained seizure freedom"

The term "seizure free" means freedom from all seizures, including auras. While the goal is no seizures for the rest of a child's life, this is unrealistic. Therefore, the International League Against Epilepsy developed a "rule of three" for calculating seizure freedom. The "rule of three" means that the child has zero seizures for a time period that is at least three times that of the longest period of seizure freedom prior to drug use, or twelve months, whichever is longer.

No seizures (including those induced by fever or sleep deprivation) can occur during this time frame; however, a seizure caused by failure to take a drug on time (noncompliance) does not count.

If your child has failed two drugs as outlined above, it's time to request a referral for an epilepsy surgery evaluation.