patients, social considerations may dictate treatment after a single seizure.

Medication Therapy

If seizures are recurrent, the goal of treatment is complete seizure freedom. In the United States, as of 2013, there were 25 AEDs in standard use to treat epilepsy with several other medications sometimes used as adjuncts. There is no perfect AED; all have potential toxic side effects and idiosyncratic reactions. For over one half of people with epilepsy the appropriate AED for their type of seizures can be completely effective and well tolerated. However, for about one quarter of people with epilepsy, no AED or combination of AEDs is completely effective. Once the seizure type and epilepsy syndrome is determined, an initial and, if needed, subsequent AED, should be chosen based on both its anticipated efficacy and toxicity profile. All AEDs can cause sedation, cognitive dysfunction, and incoordination in some patients, especially at high levels. Various rare, sometimes life threatening, reactions can occur with all of the AEDs. Commonly encountered situations are:

Idiopathic generalized epilepsy (CAE, JME, others)

- In all idiopathic generalized epilepsies, valproate or lamotrigine are the first line agents and result in complete seizure control in 85% to 90% of patients.
  - Valproate tends to cause weight gain and has been associated with the development of polycystic ovary syndrome, particularly in adolescent females. It results in hair loss in about 5%. It has an increased risk of teratogenicity.
  - Lamotrigine has a small but significant risk of a severe rash (e.g., toxic epidermal necrolysis, Stevens Johnson syndrome) for about the first 2 months after starting. A slow dose escalation substantially lowers this risk. Lamotrigine's metabolism is substantially inhibited by valproate, so in combination, lower doses of lamotrigine are required. Occasionally lamotrigine worsens myoclonus, but it is effective in most cases of JME.
- Second line options include clobazam, topiramate, levetiracetam, and zonisamide.
- In childhood absence epilepsy with exclusively absence seizures, ethosuximide should be the first choice. If any convulsions have occurred, valproate or lamotrigine should be used.
- If there is a history of more than 5 minutes of crescendo absences or myoclonus (often described as a "foggy" state) culminating in a convulsion, then oral benzodiazepines (lorazepam or diazepam) can abort the cluster and prevent a convulsion.
- Absences and myoclonus can be exacerbated by carbamazepine, oxcarbazepine, and GABAergic compounds including gabapentin, pregabalin, and tiagabine. These AEDs should be avoided in idiopathic generalized epilepsy.

Focal Epilepsy

- Almost all of the AEDs (except ethosuximide) can be effective in focal epilepsy. The choice of the first AED should be guided by side effect concerns and pharmacokinetics.
- Phenytoin is the most commonly used AED in focal epilepsy in developed countries. It is typically loaded in the emergency room after the initial seizures and subsequently continued. However, phenytoin has substantial short- and long-term toxicity and its levels are difficult to regulate due to saturation kinetics and multiple drug interactions. Its toxicities include hirsuitism, coarsening of features, and gingival hyperplasia, especially in children and adolescents. Long-term toxicities include osteomalacia, peripheral neuropathy, and cerebellar degeneration with permanent incoordination. Peak level toxicities include nystagmus, gait instability, ataxia and, if the level rises above 50, acute cerebellar degeneration and cardiac arrhythmias.
- Carbamazepine, oxcarbazepine, topiramate, levetiracetam, lamotrigine, and zonisamide are currently used as first line therapy for partial seizures. Carbamazepine and oxcarbazepine can cause hyponatremia. Topiramate can lead to weight loss (often desired), but also has undesirable cognitive side effects and predisposes to renal stones. Levetiracetam can cause severe mood changes and marked sedation, but is usually well tolerated. Lamotrigine needs to be titrated slowly due to the rash risk. Zonisamide, which also predisposes to renal stones, has a long half-life (48 to 72 hours) so is a good option for intermittently noncompliant patients.
- Patients of Asian ancestry should be tested for the HLA-B*1502 allele and patients of Northern European ancestry tested for the HLA-A*3101 allele prior to initiating treatment with carbamazepine, oxcarbazepine, and eslicarbazepine. Patients with these alleles are at increased risk of Stevens Johnson syndrome and toxic epidermal necrolysis when exposed to these drugs.
- Adjunctive treatment for partial seizures includes clobazam, valproate, pregabalin, lacosamide, gabapentin, perampanel, and primidone. The proportion of gabapentin absorbed decreases with increasing dose, which limits its effectiveness. For most, pregabalin is a better choice. Primidone is rapidly converted to phenobarbital by some people, limiting its use.
- Phenobarbital is the most widely used AED in the world due to its low cost. However, it causes sedation and cognitive impairment, and it should be avoided except in difficult to control epilepsy. The exception is neonatal seizures where it is the most commonly accepted AED.

Symptomatic generalized epilepsy (LGS, others)

- All AEDs have a role in the treatment of symptomatic generalized epilepsy, but seizure freedom is rarely achieved. At a minimum, control of the more severe seizures, including drop seizures and convulsions should be the target of therapy. Polytherapy is usually required.
- Valproate is commonly the initial medication instituted.
- Added efficacy can occur with clobazam, lamotrigine, topiramate, levetiracetam, rufinamide, and zonisamide.
- Felbamate may be effective, but its use should be limited to epileptologists due to the significant risk of fatal aplastic anemia and liver failure.
- The vagus nerve stimulator (see later) has a specific role in reducing the severity of seizures in this condition.
- Dravet syndrome and possibly the related syndrome of GEFS+ respond best to topiramate, levetiracetam, and benzodiazepines. Some drugs, including lamotrigine and phenytoin, worsen Dravet syndrome.