Dosing of AEDs must be done with care. Only a few of the AEDs are safe to load or start at a full therapeutic dose. Most should be started with a gradual dose escalation. Management guidelines are: (1) The type of seizures and epilepsy should be defined and the preferred medication should be given in usual doses and then increased until seizure control is complete or side effects occur (Table 118-4); (2) If seizures persist at toxic levels, or if major side effects occur, another agent should be tried; (3) Do not stop one agent until another has been added. Otherwise, status epilepticus may occur; (4) If seizures persist after two agents have been given to toxic levels, consider referral to a specialized epilepsy center for complex combination therapy and video-EEG long-term monitoring; (5) Toxic levels of some AEDs (e.g., phenytoin and carbamazepine) can cause seizures; (6) Extended release and longer acting AEDs are preferred for most patients; (7) Patients should be counseled to adhere to the medication regimen. Pill boxes should be encouraged. Medication noncompliance is a leading cause of poor seizure control.

Epilepsy Surgery

In most patients, epilepsy is controlled with medication. When seizures cannot be controlled by adequate trials of two appropriate single agents or by the combination of two agents, the epilepsy is termed *medically intractable* (or *refractory*), a situation encountered in approximately 25% of patients with symptomatic focal epilepsy. Such patients are at risk for the consequences of seizures: inability to drive; stigmatization by schools, employers, and families; and threats to personal educational and occupational goals. In appropriately selected cases, epilepsy surgery can abolish seizures with restoration of normal neurological function. The accurate localization of a small, safely resectable seizure focus requires intensive investigation at a specialized center.

Dietary Therapy

The *ketogenic diet* is a very high fat diet with restricted carbohydrates and protein carefully designed to cause a ketotic state mimicking starvation, but supplying adequate nutrition. It is mainly used in developmentally delayed children with severe symptomatic generalized epilepsy. The ketogenic diet can be effective in this most refractory form of epilepsy, resulting in seizure-freedom in 15% to 20%. However, the diet is hard to maintain and requires a dedicated, cooperative caregiver and a specially trained dietician.

The *modified Atkins diet* (MAD) and *low glycemic-index diet* are scaled-down versions of the ketogenic diet with mainly carbohydrate restriction. These diets are more palatable than the ketogenic diet and can be tolerated by adults. The slight ketosis achieved sometimes results in a dramatic seizure reduction in any form of epilepsy.

Neurostimulators

The *vagus nerve stimulator* is an implanted device similar in appearance to a cardiac pacemaker. The stimulating electrode is placed on the left vagus nerve in the neck and programmed to stimulate the nerve for 30 seconds every 3 to 5 minutes. Swiping a magnet over the device gives an extra stimulation that can sometimes abort a seizure. In up to two thirds of patients, partial seizures are reduced by 50% or more and seizure intensity decreases.

Another strategy in medically refractory focal epilepsy is the *responsive neurostimulator.* Chronically implanted electrodes at the seizure foci are used to rapidly detect seizure onset and abort the seizure within a few seconds by delivering an electrical stimulation directly to the seizure focus. *Deep brain stimulation* to the bilateral anterior nuclei of the thalami may also improve seizure control.

Status Epilepticus

Status epilepticus can occur with partial or generalized epilepsy and is defined as prolonged or rapidly recurring seizures without full intervening recovery. *Acute repetitive seizures* are defined as a cluster of seizures over minutes to hours with intervening recovery.

Convulsive status epilepticus (Grand mal, major-motor) is a medical emergency. Continuous generalized epileptic activity can damage the brain permanently. The most frequent cause is abrupt withdrawal of AEDs (e.g., noncompliance) in a person with known epilepsy. Other precipitants include withdrawal of alcohol or drugs in a habitual user, cerebral infection, trauma, hemorrhage, and brain tumor.

TABLE 118-4 FREQUENTLY PRESCRIBED ANTIEPILEPTIC DRUGS

NONPROPRIETARY AED NAME	ADULT TOTAL DOSE PER DAY	DOSE FREQUENCY (IN HOURS)	"THERAPEUTIC" CONCENTRATIONS
Carbamazepine	800-1600 mg	6-8 (12 for sustained release)	6-12 μg/mL
Ethosuximide	750-1500 mg	8-12	40-100 μg/mL
Gabapentin	900-3600 mg	6-8	Uncertain
Lacosamide	200-600 mg	12	Uncertain
Lamotrigine*	100-800 mg	12	2-15 μg/mL
Levetiracetam	500-3000 mg	12	15-45μg/mL
Clobazam	20-60 mg	12	Uncertain
Oxcarbazepine	600-2400 mg	8-12	15-45μg/mL
Phenobarbital	60-240 mg	24	15-40 μg/mL
Phenytoin	200-600 mg	24	10-20 μg/mL
Pregabalin	100-600 mg	8-12	Uncertain
Topiramate	50-600 mg	12	2-20 μg/mL
Valproate	500-6000 mg	8 (12-24 for sustained release)	50-120 μg/mL
Zonisamide	100-600 mg	24	Uncertain

*Slow initial dose titration mandatory for lamotrigine and often indicated for other agents.