intake and seizures, and they should be encouraged to modify their drinking habits accordingly. There are also relatively rare cases of patients with seizures that are induced by highly specific stimuli such as a video game monitor, music, or an individual's voice ("reflex epilepsy"). Because there is often an association between stress and seizures, stress reduction techniques such as physical exercise, meditation, or counseling may be helpful.

ANTIEPILEPTIC DRUG THERAPY

Antiepileptic drug therapy is the mainstay of treatment for most patients with epilepsy. The overall goal is to completely prevent seizures without causing any untoward side effects, preferably with a single medication and a dosing schedule that is easy for the patient to follow. Seizure classification is an important element in designing the treatment plan, because some antiepileptic drugs have different activities against various seizure types. However, there is considerable overlap between many antiepileptic drugs such that the choice of therapy is often determined more by the patient's specific needs, especially his or her assessment of side effects.

When to Initiate Antiepileptic Drug Therapy Antiepileptic drug therapy should be started in any patient with recurrent seizures of unknown etiology or a known cause that cannot be reversed. Whether to initiate therapy in a patient with a single seizure is controversial. Patients with a single seizure due to an identified lesion such as a CNS tumor, infection, or trauma, in which there is strong evidence that the lesion is epileptogenic, should be treated. The risk of seizure recurrence in a patient with an apparently unprovoked or idiopathic seizure is uncertain, with estimates ranging from 31 to 71% in the first 12 months after the initial seizure. This uncertainty arises from differences in the underlying seizure types and etiologies in various published epidemiologic studies. Generally accepted risk factors associated with recurrent seizures include the following: (1) an abnormal neurologic examination, (2) seizures presenting as status epilepticus, (3) postictal Todd's paralysis, (4) a strong family history of seizures, or (5) an abnormal EEG. Most patients with one or more of these risk factors should be treated. Issues such as employment or driving may influence the decision whether to start medications as well. For example, a patient with a single, idiopathic seizure whose job depends on driving may prefer taking antiepileptic drugs rather than risk a seizure recurrence and the potential loss of driving privileges.

Selection of Antiepileptic Drugs Antiepileptic drugs available in the United States are shown in Table 445-8, and the main pharmacologic characteristics of commonly used drugs are listed in Table 445-9. Worldwide, older medications such as phenytoin, valproic acid, carbamazepine, phenobarbital, and ethosuximide are generally used as first-line therapy for most seizure disorders because, overall, they are as effective as recently marketed drugs and significantly less expensive overall. Most of the new drugs that have become available in the past decade are used as add-on or alternative therapy, although many are now being used as first-line monotherapy.

TABLE 445-8 SELECTION OF ANTIEPILEPTIC DRUGS

Generalized-Onset Tonic-Clonic	Focal	Typical Absence	Atypical Absence, Myoclonic, Atonic
First-Line			
Lamotrigine	Lamotrigine	Valproic acid	Valproic acid
Valproic acid	Carbamazepine	Ethosuximide	Lamotrigine
	Oxcarbazepine	Lamotrigine	Topiramate
	Phenytoin		
	Levetiracetam		
Alternatives			
Zonisamide[a]	Topiramate	Lamotrigine	Clonazepam
Phenytoin	Zonisamide[a]	Clonazepam	Felbamate
Carbamazepine	Valproic acid		Clobazam
Oxcarbazepine	Tiagabine[a]		Rufinamide
Topiramate	Gabapentin[a]		
Phenobarbital	Lacosamide[a]		
Primidone	Exogabine[a]		
Felbamate	Phenobarbital		
	Primidone		
	Felbamate		

[a]As adjunctive therapy.

In addition to efficacy, factors influencing the choice of an initial medication include the convenience of dosing (e.g., once daily versus three or four times daily) and potential side effects. In this regard, a number of the newer drugs have the advantage of reduced drug-drug interactions and easier dosing. Almost all of the commonly used antiepileptic drugs can cause similar, dose-related side effects such as sedation, ataxia, and diplopia. Long-term use of some agents in adults, especially the elderly, can lead to osteoporosis. Close follow-up is required to ensure these side effects are promptly recognized and reversed. Most of the older drugs and some of the newer ones can also cause idiosyncratic toxicity such as rash, bone marrow suppression, or hepatotoxicity. Although rare, these side effects should be considered during drug selection, and patients must be instructed about symptoms or signs that should signal the need to alert their health care provider. For some drugs, laboratory tests (e.g., complete blood count and liver function tests) are recommended prior to the institution of therapy (to establish baseline values) and during initial dosing and titration of the agent. Importantly, studies have shown that Asian individuals carrying the human leukocyte antigen allele, HLA-B*1502, are at particularly high risk of developing serious skin reactions from carbamazepine and phenytoin. As a result, racial background and genotype are additional factors to consider in drug selection.

ANTIEPILEPTIC DRUG SELECTION FOR FOCAL SEIZURES Carbamazepine (or a related drug, oxcarbazepine), lamotrigine, phenytoin, and levetiracetam are currently the drugs of choice approved for the initial treatment of focal seizures, including those that evolve into generalized seizures. Overall they have very similar efficacy, but differences in pharmacokinetics and toxicity are the main determinants for use in a given patient. For example, an advantage of carbamazepine (which is also available in an extended-release form) is that its metabolism follows first-order pharmacokinetics, which allows for a linear relationship between drug dose, serum levels, and toxicity. Carbamazepine can cause leukopenia, aplastic anemia, or hepatotoxicity and would therefore be contraindicated in patients with predispositions to these problems. Oxcarbazepine has the advantage of being metabolized in a way that avoids an intermediate metabolite associated with some of the side effects of carbamazepine. Oxcarbazepine also has fewer drug interactions than carbamazepine. Lamotrigine tends to be well tolerated in terms of side effects. However, patients need to be particularly vigilant about the possibility of a skin rash during the initiation of therapy. This can be extremely severe and lead to Stevens-Johnson syndrome if unrecognized and if the medication is not discontinued immediately. This risk can be reduced by the use of low initial doses and slow titration. Lamotrigine must be started at lower initial doses when used as add-on therapy with valproic acid, because valproic acid inhibits lamotrigine metabolism and results in a substantially prolonged half-life. Phenytoin has a relatively long half-life and offers the advantage of once or twice daily dosing compared to two or three times daily dosing for many of the other drugs. However, phenytoin shows properties of nonlinear kinetics, such that small increases in phenytoin doses above a standard maintenance dose can precipitate marked side effects. This is one of the main causes of acute phenytoin toxicity. Long-term use of phenytoin is associated with untoward cosmetic effects (e.g., hirsutism, coarsening of facial features, gingival hypertrophy) and effects on bone metabolism. Due to these side effects, phenytoin is often avoided in young patients who are likely to require the drug for many years. Levetiracetam has