The hydantoins are cumulative in effect; therefore, the dosage schedule must be adjusted gradually over a long period to obtain control without producing toxic reactions. Ordinarily, a hydantoin should be added to a regimen after an initial trial with the relatively safer **phenobarbital** has not provided adequate control. Alternatively, many clinics and some of the Council's consultants prefer **diphenylhydantoin** as the initial drug. The Council's moderate preference for **phenobarbital** is based on considerations of relative safety, although this drug does introduce the inconvenience of drowsiness for many patients. Other drugs can be added if a combination of a hydantoin and **phenobarbital** do not completely control the seizures. **Primidone** [MYSOLINE] ordinarily should not be *added* to this regimen, but it may be *substituted* for the **phenobarbital** in refractory epilepsy of the major motor and psychomotor types. Also, psychomotor epilepsy may respond to **methsuximide** [CELONTIN]. **Phenacemide** [PHENURONE] may be effective in controlling psychomotor or various other seizures, but since it is extremely toxic, it is only of limited usefulness and should be used only if other medications are ineffective. Inorganic bromides (**eg, sodium bromide, potassium bromide**) also have anticonvulsant activity against grand mal, but because of their toxicity, interest in them is chiefly historical. However, they may have a limited place in the treatment of children with grand mal.

**Methsuximide** [CELONTIN], **phensuximide** [MILONTIN], **ethosuximide** [ZARONTIN], **trimethadione** [TRIDIONE], and **paramethadione** [PARADIONE] are useful primarily in the treatment of petit mal. **Ethosuximide** is the drug of choice in this group, but **phensuximide** may be considered for initial treatment in mild cases because it is moderately safer. **Acetazolamide** [DIAMOX], and perhaps ketogenic diets, control petit mal in some patients. Recently, selected new benzodiazepine derivatives, particularly **diazepam** [VALIUM], have also shown promise and relative safety. Among the remaining drugs, **trimethadione** is probably the most likely to be effective, but it is also the most dangerous. Petit mal rarely responds to **phenobarbital** alone; nevertheless this drug, because of its broad anticonvulsant spectrum, should be tried initially unless there is convincing evidence, including a characteristic electroencephalogram, that the patient has classical petit mal uncomplicated by any other type of seizure. Less satisfactory agents like **meprobamate** [EQUANIL, MILTOWN], **quinacrine** [ATABRINE], or the amphetamines may be tried if other medications do not control petit mal. For patients who have petit mal and other seizure types, drugs effective in controlling those other types must be combined with the drugs selected for the treatment of petit mal.

Minor motor seizures are akinetic and myoclonic types that are often refractory to drug therapy. They may occur alone or in association with petit mal or grand mal. Drugs effective for both seizure types may be used alone or in combination. The minor motor seizure syndrome of infancy or childhood sometimes responds to **corticotropin** or adrenocortical steroid therapy or to a ketogenic diet program. Recent experience with various benzodiazepine derivatives indicates that some of the compounds in this group have effectiveness in minor motor epilepsy; of the benzodiazepine derivatives currently marketed in this country, **diazepam** [VALIUM] has given the most favorable results.

Sometimes, epileptic seizures that apparently are under good control by drugs will escape from control. When a barbiturate or hydantoin is involved, the escape may result from a physiologic adjustment in which the patient's metabolism of the drug is increased. With these particular drugs, an increase in dosage will ordinarily reestablish control, and once this is accomplished, there is no reason to expect a repetition of the escape unless the disease itself happens to worsen. Trauma or emotional stress may cause an increase in the dosage requirement, which should be borne in mind if a patient requires surgery.

Spontaneous remissions, particularly of petit mal seizures, are common if convulsive disorders have begun during childhood but are rare if they have begun during adulthood. Anticonvulsant therapy therefore must be prolonged; as a rule, drugs are continued until the patient has been completely free of seizures for two to four years. When a decision is made to discontinue their administration, the dosage of one drug at a time should be reduced gradually, since sudden withdrawal of any of these drugs may precipitate a recurrence of seizures or even status epilepticus. However, when a serious adverse reaction to a drug occurs, the agent should be discontinued immediately and another anticonvulsant should be given to protect the patient during this period.

Status epilepticus is a serious emergency that requires prompt and vigorous treatment to prevent permanent harmful effects or death. It may be terminated by the intravenous administration of **phenobarbital.** This drug is preferable to shorter acting barbiturates, since its effect is practically as rapid but lasts longer. The full calculated anticonvulsant dose should be given initially since the use of fractional doses may result in the paradoxic situation of drug-induced depression but continued status epilepticus. **Diphenylhydantoin** [DILANTIN] may be given intravenously or intramuscularly, but its onset of action is delayed for 5 to 15 minutes. It has the advantage of usually not depressing respiration, but intravenous administration must be slow to avoid serious hypotension. Recently **diazepam** has been shown to be effective when given parenterally. **Paraldehyde** given parenterally is still used occasionally. When anesthetic agents are necessary, they should be given under the supervision of an anesthesiologist, when possible, and resuscitative equipment should be available.