Major motor seizures, usually with severe, protracted, clonic convulsions, are sometimes associated with the withdrawal syndrome in persons with physical dependence on barbiturates, alcohol, or certain other sedative drugs. Barbiturates will often help prevent these dangerous convulsions; the hydantoins are usually of little value.

Adverse Reactions and Precautions

Many minor reactions to anticonvulsant drugs may be overcome by reducing the dosage of the responsible agent, which may, however, necessitate the addition of another anticonvulsant agent to the regimen.

Most anticonvuisants produce gastrointestinal disturbances in at least some patients, especially during the early stages of treatment. The symptoms may be reduced either by administering the drugs after meals or by decreasing the dosage.

Many of the anticonvulsants have sedative effects, and drowsiness is sometimes a significant complaint. Again, this effect is most noticeable during the early period of treatment; if it persists, a reduction of dosage may be indicated. Sedative drugs may cause alterations in mood, which occasionally are serious (see the chapter on Sedatives and Hypnotics).

Other anticonvulsants also can cause mental disturbances. **Phenacemide** [PHENURONE] is particularly prone to cause serious personality changes including psychoses and suicidal depressions.

Ataxia occurs commonly with the hydantoins and, if persistent, requires reduction in dosage. There is evidence that the hydantoins can cause cerebellar damage if a dosage that produces ataxia is administered for a prolonged time. For practical purposes, however, this danger appears remote since the reaction is so troublesome in itself that it demands correction by dosage adjustment. Very young patients can present an exception, as drug-induced ataxia may be confused with the natural unsteadiness of the toddler. Ataxia also may occur with the use of barbiturates.

Many anticonvulsants commonly cause skin eruptions, which are usually morbilliform or acne-like and may disappear when the dosage is reduced or the drug is temporarily discontinued and cautiously readministered. However, a skin reaction may herald the development of a severe reaction that may warrant withdrawal of the drug. Lupus erythematosus, Stevens-Johnson syndrome, angioneurotic edema, serum sickness, and polyarteritis have been associated with anticonvulsant medication. Anaphylaxis is extremely rare. Other reactions that occasionally have been noted with some anticonvulsants include alopecia and hypertrichosis.

Because the barbiturates are particularly prone to aggravate porphyria, their use should be avoided in patients with that disease.

Several of the anticonvulsant drugs may cause reversible visual disturbances such as diplopia and nystagmus; one of the most notable, hemeralopia (defective vision in a bright light), occurs with the oxazolidinediones, **trimethadione** [TRIDIONE] and **paramethadione** [PARADIONE].

Certain untoward effects are frequently characteristic of a particular anticonvulsant and may not occur with a chemically related drug; for example, **diphenylhydantoin** [DILANTIN] frequently causes gingival hyperplasia, but this reaction seldom occurs with **mephenytoin** [MESANTOIN], and apparently never with **ethotoin** [PEGANONE].

Lymphadenopathies simulating malignant lymphomas have occurred with several of the anticonvulsant drugs. Hydantoins have been implicated most frequently. Although it is questionable whether **diphenylhydantoin** is as prone to cause these pseudolymphomas as is **mephenytoin,** it is responsible for a greater number of reactions since it is more widely used. The signs and symptoms may show a temporary progression but usually begin to disappear within one to two weeks after therapy is stopped. A few cases of true lymphoma and of Hodgkin's disease have been reported in which a causal relationship to hydantoin therapy seems possible.

Megaloblastic anemias, which respond to **folic acid** or **leucovorin** (folinic acid) therapy, also have been reported with several anticonvulsants. Accordingly, periodic blood studies are indicated when such drugs are taken. Usually, the drug may be continued if the anemia responds well to treatment. However, because of the possibility that **folic acid** may interfere with the anticonvulsant action, routine prophylactic treatment with **folic acid** in patients without anemia is not suggested.

Among the most dangerous reactions that develop during therapy with anticonvulsant drugs are those that result from damage to the marrow, liver, and kidneys. Severe blood dyscrasias have sometimes been associated with **phenacemide** [PHENURONE], **mephenytoin** [MESANTOIN], **paramethadione** [PARADIONE], **trimethadione** [TRIDIONE], and less frequently with other drugs. Baseline blood counts should be made before initiating treatment with these drugs. Although periodic blood studies during treatment will detect mild leukopenias of uncertain clinical significance, they cannot be relied upon to predict the more serious reactions that ordinarily occur precipitously (eg, agranulocytosis, thrombocytopenia, aplastic anemia). There is some chance that an aplastic anemia might be detected early, before symptoms develop, if one were so fortunate as to have a hemoglobin determination at a time during its beginning decline, but even moderate expectation of such detection would require an impractical frequency of blood studies in view of the extreme rareness of the reaction with most drugs. Since early recognition of the presence of a dyscrasia and discontinuance of the offending drug are essential, the patient should be advised to report promptly such symptoms as sore throat, fever, easy bruising, petechiae, epistaxis, or other signs of an infection or bleeding