tendency. Clinical and laboratory evaluation is necessary if such symptoms occur. Although the risk of dyscrasias is diminished after the first year of treatment with these medications, the physician should be constantly alert to their possible occurrence at any time. The mortality rate from aplastic anemia is particularly high and, if the patient does survive, recovery is slow. Except for **mephenytoin** and **phenacemide,** however, this reaction is fortunately very rare with the anticonvulsants that cause it at all.

Severe liver disease, sometimes fatal, has occurred with **phenacemide** [PHENURONE] and more rarely with some of the other anticonvulsants, including hydantoins. Before treatment with these drugs is begun, it is advisable to make baseline liver function studies, and patients should be instructed to report promptly any symptoms of hepatitis such as jaundice, dark urine, anorexia, abdominal discomfort, or other gastrointestinal symptoms. Since this drug-induced hepatitis is probably idiosyncratic, the monitoring of treatment with periodic laboratory studies in asymptomatic patients is of doubtful reliability in predicting a reaction. **Phenacemide** may present an exception, as there is some evidence that hepatitis can develop insidiously with its use; liver function abnormalities, eg, decreased prothrombin activity, may herald serious disease.

Nephropathies have developed occasionally during treatment with anticonvulsants, especially in patients receiving the oxazolidinediones, **trimethadione** and **paramethadione.** Unlike the blood dyscrasias and hepatitis, these reactions may develop insidiously without producing symptoms in the early stages. Therefore, urinalyses should be made before treatment and periodically during treatment. The development of any significant renal abnormality is an indication for discontinuing the drug.

From the preceding discussion, the question arises of just what type of laboratory monitoring is advisable for patients taking anticonvulsants who have no symptoms suggesting marrow, hepatic, or renal damage. As noted, baseline studies of the functional state of these organs are needed before initiating treatment with drugs known to cause damage even occasionally. Tests should be repeated and perhaps extended if signs or symptoms of a reaction develop. Periodic urinalyses and evaluations for anemia are of value with drugs known to cause nephropathy or megaloblastic anemia, as these conditions may occur well in advance of their symptoms. The problem is whether to subject patients to frequent testing for idiosyncratic blood dyscrasias and hepatitis when nothing suggests the presence of these disorders. The Council's consultants have expressed widely divergent views on whether such testing is of any significant medical value with most anticonvulsants. It is known that various minor laboratory abnormalities may appear and cannot be relied upon to herald the development of a serious reaction. Moreover, when a dangerous idiosyncratic reaction does occur, signs or symptoms will probably appear about as soon as a diagnosis can be made reliably by laboratory methods (with the possible exceptions of hepatitis from **phenacemide,** and aplastic anemia from **mephenytoin** and **phenacemide**). Accordingly, and with due respect to those consultants who disagree, the Council regards routine laboratory monitoring with most drugs as optional, rather than mandatory, if the only issue is whether an asymptomatic patient is taking a drug that rarely produces a blood dyscrasia or hepatitis by some apparently idiosyncratic mechanism. This is in contrast with the situation where a drug has a direct toxic action on the marrow or liver.

A frequently cited paradoxic effect of anticonvulsants is the tendency of agents effective for one type of seizure to aggravate or precipitate seizures of another type. However, epileptic disorders tend to be mixed as to seizure type and, very probably, the apparent aggravation of one type is a manifestation of the natural course of the disease and merely reflects the therapeutic ineffectiveness of the particular drug for that type of seizure. Causally related precipitation of seizures by anticonvulsant drugs probably is rare, and some consultants doubt that it occurs. There is no question, however, that abrupt withdrawal of anticonvulsants can precipitate seizures. Thus, when a drug is to be discontinued, the dosage should be reduced gradually unless rapid withdrawal and substitution of another drug is mandatory because of a serious adverse reaction.

In general, there has been little systematic investigation of the anticonvulsant drugs for teratogenic effects, but a lack of reported teratogenicity after extensive use provides some circumstantial evidence of probable safety. Thus, whenever practical, it would seem prudent to use older and more extensively used anticonvulsants if it is necessary to treat epilepsy in a pregnant woman.

As a general rule, the more toxic compounds should not be used if an equally effective and less potentially toxic preparation is available. However, minor adverse effects should be expected and accepted with any drug. The anticonvulsant drugs in frequent current use, and a few that are rarely used, are listed and briefly described in the individual evaluations that follow. Not every known adverse reaction is mentioned, but an effort has been made to include those that are notable because of danger to life, unusual frequency of occurrence, proneness to cause significant discomfort, or peculiarity to a particular drug.

Barbiturates

Phenobarbital

Most broadly useful anticonvulsant. Initial therapy of choice in most epilepsy (see general statement). Principal effectiveness is in major motor and psychomotor seizures. Sedative-hypnotic effect, as well as ataxia, may present problems. Produces hyperactivity in some children instead of