upon the multitude of known enzyme systems as well as those suspected or latent or subclinical, but not as yet identified, one could predict that many drug effects that are now classified as idiosyncratic or even allergic will gradually be herded in the fold of pharmacogenetic disorders or perhaps enzyme insufficiencies that are acquired as the result of disease.

DRUG INTERACTIONS

One of the more complex, fascinating, and disturbing areas of pharmacology which has direct pertinence in any discussion of adverse drug effects is "drug interactions." Efforts to establish a feasible classification continue as new mechanisms are discovered. Dr. Hartshorn defines drug interaction as—and this is the best definition I could find—"The phenomenon which occurs when the effects of one drug are modified by the prior or concurrent administration of another—or the same—drug(s). Drug interactions may arise either from alteration of the absorption, distribution, biotransformation, or excretion of one drug by another or from combination of their actions or effects."

He makes a distinction between interaction and drug incompatibility. He reserves the latter form for reactions which occur either in the bottle as one mixes two drugs or in the syringe before they are given to a patient.

Dr. Irey has also been involved in interaction and he lists another classification of interaction in categories.

1. Interaction with other drugs or themselves. This is an induction process.
2. Then there may be interaction with endogenous physiologic chemical agents. And the example here is monoaminoxidase inhibitors and epinephrine.
3. Interaction of the drug with components of the diet, as in the administration of MAOI drugs with tyramine as one would get in cheddar cheese.
4. Interactions with chemicals used in diagnostic tests or the results of such tests. And an example of this would be the oral contraceptives which may modify the glucose tolerance tests.

Two of the more fascinating aspects of drug interactions have to do with enzyme induction and enzyme inhibition, and I would like to discuss these briefly, in turn, just to illustrate the magnitude of the problem.

ENZYME INDUCTION

Many drugs, when taken over a period of time, can cause a marked acceleration of their own metabolism or can accelerate the metabolism of other drugs being administered concomitantly or subsequently. This effect is mediated through stimulation of drug metabolizing enzymes in the liver. This process is called "enzyme induction," and it has become an extremely important aspect of drug toxicity. Induction can lead to an escalating requirement for maintenance doses of a given drug, each of which can be acutely toxic.

Fortunately, most drugs do not involve enzyme induction, but it must be conceded that not all drugs have been subjected to this rather difficult and time-consuming type of testing. Nor is it known if all individuals are susceptible to enzyme induction by a specific drug.

And this brings us to another aspect of this effect. Not only may a