

The problems of adverse drug effects are many. Reduced to simplest elements, when drug A is introduced into the body, ultimately it or its intermediate products will be carried in blood and body fluids to bathe virtually all cells of the organism.

The effects of drug A become perceptible only when the function of certain organs is modified, by whatever mechanism, and this may be either beneficially or detrimentally, to the point of producing clinically perceptible changes, and it is by these phenomena that we learn to characterize the nature of drug A.

Yet as we focus attention upon the anticipated response of a specific organ (or organs), we are inclined to forget that drug A is also in contact with other tissues of the organism. Effects in these areas are not in immediate evidence, but subtle often nefarious influences may be at work, which become manifested clinically, at a much later date.

Such long-range effects may never be correlated with the antecedent administration of our drug A and if one were to add drugs B, C, D, E, F, and so forth, one begins to appreciate the endless combinations and permutations.

The identification of a significant adverse reaction follows a long but familiar pattern. First, scattered unsubstantiated reports—and these may come by hearsay, anecdote, word of mouth, in the cloakroom at the hospital—are encountered, hinting that a certain drug has caused a certain undesirable effect.

Then begins the tedious process of painstaking retrospective analysis. Many suspected cases must be scrutinized, and perhaps, ultimately the suspected culprit—the provocative drug will be revealed.

To depart from the text, there are several mechanisms whereby this is done. The most familiar, of course, is the FDA gathering of their forms 1639 where any physician, who encounters an adverse reaction may complete the form and send it to the FDA where it will be plugged into their computer system. The AMA Council on Drugs also collects similar types of reports from private physicians throughout the country, which again will be introduced to their computer. And if physicians in the North, South, East, or West, all unrelated and unknown to each other, seem to report the same kind of reaction occurring with a specific drug, then the wheels are set into motion for the beginning of an investigation.

Senator NELSON. May I interrupt you a moment?

Dr. MOSER. Yes.

Senator NELSON. How effective is the reporting system, that is, what percentage of the doctors around the country who discover a side effect from using a drug, report it to the FDA or AMA Council on Drugs?

Dr. MOSER. Senator, if you will bear with me, I will get to that toward the end.

At this point one must follow with a meticulously controlled prospective study which will involve provocative testing in animals and often in men, before we can prove that indeed it was the suspected drug that causes this difficulty. It is a tedious, frequently unrewarding process. But it is the only valid technique currently available to medicine.

This is a shadow world of pathophysiology, where relation of cause to effect is at best difficult to assess. I need only cite the still raging