

controversy over analgesics and renal disease to demonstrate this difficulty, and there are other problems.

Perhaps the most careful, definitive study of adverse drug reactions is being conducted by Dr. Nelson Irey of the recently established Registry of Tissue Reactions to Drugs. In reviewing the first 509 cases discussed in the new registry, Dr. Irey cited four principal areas of difficulty in his investigations.

Senator NELSON. Who established the Registry of Tissue Reactions to Drugs?

Dr. MOSER. This was a joint effort, as I understand it, sir. The registry is sponsored by AMA, Food and Drug Administration, PMA, and NIH. But the organization operates independently, and Dr. Irey is an outstanding scientist. They were in the old Army Institute of Pathology, and at the present time they are in interim headquarters, and I am told that they will occupy a wing at the new Armed Forces Institute of Pathology on the campus at Walter Reed when that building is completed. That is where the new headquarters for the Armed Forces Medical Museum will be. Dr. Irey told me several months ago that that is where they ultimately will keep their registry.

So it is a very independent organization. I think it is a fine study.

Dr. Irey cited in one of his publications four principal areas where he is having difficulty identifying these types of reactions. One, there is incomplete time relationship between the drugs and the disease. Second, in most instances there is a multiplicity of drugs administered (this makes it difficult to pin down which drug or drugs is involved). Often there is a lack of objective means of demonstrating a correct relationship between the drug and the reaction.

And, finally, there is a limited number of reaction patterns of the body to the entire range of physical, chemical, and biologic causes of disease.

In other words, the body has a restricted number of ways in which it can respond to harmful stimuli regardless of their source whether it is bacteria or a drug or a climatic condition, et cetera.

The liver, for example, can only respond in a limited number of ways. Very frequently it is extremely difficult to say whether a drug or a virus has been the cause of a specific liver dysfunction, such as hepatitis.

Thus, following the appropriately rigid criteria demanded by the registry, it was observed that in only 8 percent could a specific drug be definitely called the causative factor. In 40 percent it was considered to be "probable"; in 32 percent "impossible"; and in 15 percent, "coincidental." In 4 percent there was no apparent relationship. The contribution of drug interactions to this complex milieu will be discussed later.

The widely quoted adverse reaction studies of Cluff and associates at the Johns Hopkins Hospital has pointed up dramatically, the "iceberg" nature of this problem. This was an intensive prospective assault on the question, conducted by highly motivated house officers; 714 such patients with adverse drug reactions were discovered during a 3-month period at the Hopkins.

Cluff has stated that 13.6 percent of patients acquired an adverse drug reaction during the period of hospitalization, and the other results that he found were also rather astonishing.