Dr. MOSER. Yes.

Mr. GORDON. These are also sold over the counter without a prescription? Isn't that right?

Dr. MOSER. Most of them have had phenacetin removed, according to my information. I think there may be a few companies that still produce it, but I think most of the APC's have the phenacetin removed.

Now, I want to say that this is a far from settled business. I don't mean to sit here and tell you that I know the answer to this problem, because many fine people have devoted a lot of time to trying to work this out. I don't want to take a stand on this because I really don't know. Let us say that there is perhaps an increased incidence of interstitial nephritis and papillitis in patients who have taken a variety of analgesic compounds. What the specific agent (or agents) is I don't really know.

I would like to go on to discuss now the phenomenon of delayed excretion of drugs or their active intermediate products (which we call metabolites), by an organ which is already diseased. In this situation the unanticipated high blood levels introduce a whole new spectrum of toxic effects. And what happens to the diseased kidney of itself, if the drug which it has been reticent to excrete, happens to be specifically toxic to the kidney and then becomes superconcentrated in the countercurrents of the kidney medulla.

All this means is that in the lower part of individual kidney units (in the lower part of the nephron) where there is exhaberant water absorption, any product that is coming through the kidney will be concentrated in this particular portion. And I pose the thought that in the event that the drug which with we are dealing happens to be nephrotoxic, the kidney may suddenly be receiving a very concentrated dose of this particular drug. It is an interesting area.

Or, consider the patient with a subclinical liver disease—a mild cirrhosis, if you will. What happens when he is given halothane or chlorpromazine or phenylbutazone, drugs known, occasionally, to be unkind to the normal liver? What happens when it is given to a previously diseased liver?

One could cite many examples wherein an organ with marginal function may be further insulted by a drug administered, most innocently, to treat another ailing system? The thought remains a continuing source of uneasiness in all drug therapy.

The mechanisms of adverse drug reactions have been a subject of many taxonomies, and I have selected one feasible classification as modified from a paper by Long, and he lists seven classifications:

Hypersensitivity or allergy; idiosyncrasy; immunological injury; enzyme induction (which means acceleration of the metabolism of a drug), enzyme potentiation (or inhibition of drug metabolism), carcinogenesis (which means cancer), teratogenesis and mutagenesis, which mean the induction of congenital conformities.

I don't feel it is pertinent to this presentation to delve in depth into the mechanisms of drug interactions or specific physiologic mechanisms that cause adverse reactions. However, a few general remarks may facilitate understanding of some of the problems that beset the practitioner in his effort to employ drugs effectively.