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Reports of Scientific Meetings

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Drug Information Association Symposium on Drug Interactions

During the past several years, the subject of drug interactions has received increasing attention in the medical and pharmaceutical literature. The clinical, pharmacologic, and medical communications aspects of interaction among drugs administered therapeutically were highlighted at a Symposium on Drug Interactions, Benefits and Hazards, held by the Drug Information Association in Philadelphia, Pennsylvania, on January 20 and 21, 1972. The interdisciplinary nature of the meeting brought authorities in biomedical communications and pharmacologic sciences together with clinicians, hospital pharmacists, and representatives of industry and government.

At the initial session, entitled "Mechanisms of Drug Interactions—The Problem We Face," Dr. James R. Gillette discussed general pathways of drug metabolism and indicated the various steps at which microsomal enzyme-inducing drugs and polycyclic hydrocarbon substances can affect the metabolism and pharmacologic activity of agents administered therapeutically. Dr. David G. Shand discussed different mechanisms by which one drug may interfere with the absorption, distribution, or elimination of another, and stressed the important role of concomitant disease, such as malabsorption, hepatic, renal or cardiac failure, hypoalbuminemia, etc., in influencing drug activity. The clinical significance and potential lethal and adverse affects of certain drug interactions were reviewed by Dr. Daniel Azernoff, who pointed out that loss of the therapeutic effect of a drug, as well as enhanced toxicity, may result from drug interaction. Although reduction of therapeutic efficacy may be difficult to measure quantitatively, the disease process may continue unabated as a consequence of the interaction. In a talk subtitled, "Sweet Uses of Adversity," Dr. Leo Hollister noted that interactions between drugs can sometimes produce therapeutically beneficial effects. Thus, the concurrent administration of ethanol may block the formation of a toxic metabolite of methanol, adsorbing agents such as charcoal or eggwhite can interact with ingested chemicals to impair their absorption, and the basic protein, protamine, can be used therapeutically to bind and neutralize excessive amounts of heparin, which is acidic.

At a session moderated by Dr. Elliot Vesell, the respective roles of the basic pharmacologist, the industrial researcher, the clinician and the pharmacist in discovering, investigating, observing, recording, and reporting drug interactions were discussed. Dr. Jan Koch-Weser suggested that the great majority of unexpected interactions between drugs have been discovered by astute clinicians who fortuitiously observed and recognized them in their patients. However, he stressed that chance clinical observations represent an inefficient mechanism for increasing knowledge about drug interactions, and that the magnitude and seriousness of the drug interaction problem requires increased emphasis on development of effective epidemiologic and experimental techniques for organized investigations in this field. The need for a "balanced appraisal" of the applicabiltiy of scientific studies of mechanisms of drug interactions to the practical problems of therapeutics was discussed by Dr. Murry Weiner. Dr. Richard P. Kenna indicated that the pharmacist who maintains medication records of the patients he serves is in an ideal position to observe, report and prevent drug interactions in these patients. The lack of readily accessible up-to-date information on interactions involving non-prescription medications, and the availability of these drugs from a number of sources, create special problems in dealing with drug interactions in non-hospitalized patients.

Dr. Vincent Bouchard's presentation, which concerned drug-induced modifications of laboratory test results, stressed the potential role of clinical pharmacists in recognizing, record-

ing and reporting such modifications. The interaction of environmental chemicals with drugs was the subject of Dr. Kenneth du Bois' talk, which reviewed evidence that exposure to environmental chemicals might modify patient response to therapeutic agents. Discovery of the ability of DDT and related chlorinated hydrocarbons to increase the activity of hepatic microsomal enzymes and discovery of the effects of organophosphate insecticides in inhibiting esterases that catalyse the detoxification of certain drugs establish a precedent for concern. Dr. Robert B. Forney reviewed the effects of both acute and chronic use of alcohol on drugs administered therapeutically, noting that the effects of alcohol on drug-metabolizing enzymes are complex, and that "ethanol should be used cautiously with drug therapy."

The final day's sessions concerned compiling, evaluating, organizing, and distributing information about drug interactions. The nature of the biomedical communications problem involved in dealing with drug interactions was reviewed by Miss Winifred Sewell, who reported that increasing interest in drug interactions has led to this entry's being included in *Index Medicus*. Mr. Victor Orgoni noted that the indexing of information about drug interactions has been largely ignored in the past by the secondary sources of biomedical literature informaiton, but that efforts are now under way to develop procedures for rapid computer retrieval of such data. The experiences of the Food and Drug Administration in acquiring adverse drug interaction information through a variety of surveillance techniques were reviewed by Dr. Albert Esch, and the extensive and highly productive retrospective epidemiologic investigations of the Boston Collaborative Drug Surveillance Program were described by Dr. Hershel Jick. The Boston program, which has been in operation for more than five years, has proved valuable in uncovering previously unsuspected drug interactions and in generating hypotheses for clinical and pharmacologic investigations in this area.

Dr. Dwight Tousignaut and Dr. Edward G. Feldmann described the activities of the American Society of Hospital Pharmacists and the American Pharmaceutical Association, respectively, in the collection and dissemination of drug interaction information. The activities of the ASHP focus on compilation and computerization of drug interaction references, whereas the APA project has involved extensive professional review of the scientific literatue on drug interactions and preparation of a series of monographs on this subject. Dr. Stanley Cohen described the computer-based drug interaction-warning system developed at Stanford University to deal with clinically significant drug interactions in hospitalized patients. This on-line system for prospective identification of potentially interacting drug combinations operates through computer-controlled video terminals placed in the hospital pharmacy, and provides written notification to the pharmacy, medical, and nursing staffs when a newly prescribed drug has the potential of interacting with a medication the patient is already receiving.

Although inclusion of a broad range of subjects, ranging from the basic pharmacology of drug interactions to computer methodology for dissemination of drug interaction information, precluded consideration of any single topic in depth during the two-day symposium, the meeting nevertheless presented a well-organized overview of the drug interaction problem in a highly concentrated form.

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