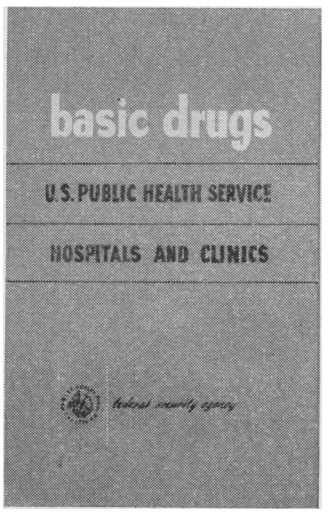
An Objective Approach to Drug Therapy

By J. SOLON MORDELL, B.A., Ph.G., and C. K. HIMMELSBACH, M.D.



In April 1952, Paul deHaen reported on pharmaceutical products introduced in the years 1948 through 1951. His report was based on a survey he made of trade and medical journals (*1*). The 1951 data are illustrative of the preceding 3 years. Among the 322 pharmaceutical products introduced by 86 manufacturing firms in 1951, there were 35 different single chemicals, or about 11 percent of the total. Also, deHaen found 74 instances of duplication of single chemicals—23 percent of the products introduced. And of especial note is this: There were 211 compounded items—66 percent of the 322 total different products introduced. In addition, there were 120 new dosage forms.

Here is telling evidence of how the word "new" has been abused in the field of drug therapy. Such abuse calls for a distinction between what is really "new" in the sense that penicillin was new in 1943 and that which is a mixture of known drugs marketed under a new name or a duplication of the "new" drug under other names.

Without knowing at what rate drugs become obsolete and unavailable, we are convinced that the net effect is the addition of more and more drugs each year. Thus, discriminate selection becomes increasingly difficult by virtue of numbers alone, and the state of confusion is compounded.

With this vast numerical growth, and the rapid progress in therapeutics—for example, cortisone, aureomycin, chloromycetin, terramycin, isoniazid, in but a few years—there comes the need for improved procedures for clinical assessment. The problem is that of devising the best method whereby the physician and the dentist may be assisted in the difficult task of selecting suitable agents from the multiplicity of drugs and drug preparations which confront them.

The professional interdependence of medicine, dentistry, and pharmacy has been recognized for a long time. We have observed, in the Public Health Service, the development of a wholesome working interrelationship among the three sciences in their common search for an objective approach to sound drug therapy and to uniform drug nomenclature. Early in 1953, the Public Health Service will release "Basic Drugs: U. S. Public Health Service Hospitals and Clinics" (*2*), a handbook of drug therapy which is in every sense a significant achievement in meaningful teamwork. The climax of 4 years' cooperative study, its publication represents a noteworthy advance in

Mr. Mordell, senior pharmacist, in the Division of Civilian Health Requirements of the Office of the Surgeon General, Public Health Service, was until January 1951 chief of the pharmaceutical service of the Public Health Service out-patient clinic, Washington, D. C. Dr. Himmelsbach is the medical officer in charge of the clinic, which is under the direction of the Division of Hospitals, Bureau of Medical Services.

the satisfying exercise of professional cooperation in trying to make some order out of a confused situation.

Can some order be achieved? How?

Valuable sources of information are available in the standard pharmacological texts and in "New and Nonofficial Remedies" of the American Medical Association; "Reports of the Council on Pharmacy and Chemistry of the American Medical Association"; "Accepted Dental Remedies" of the American Dental Association; and "Useful Drugs" of the Council on Pharmacy and Chemistry of the American Medical Association.

Formularies and other types of drug listing have been individually compiled in many hospitals. However good these listings may be for the specific purpose for which they were designed, many serve mainly as convenient references to indicate the items available in an individual institution. Often, they lack the important features of selectivity and simplification based on fundamental scientific clinical pharmacology. Furthermore, they frequently fail to include a base—a point of departure, a set of criteria—so necessary for an orderly approach to sound drug therapy.

"Standardization"

We hesitate to use the word "standardization" because to many it immediately connotes rigidity. It is therefore important to stress the fact that any plan in the direction of rationalization of drug use must be flexible, even though it does require adherence to certain fundamental principles. If this one concept is not understood and kept indelibly in view, no such plan can be effective in operation: it would lack effectiveness, for our purpose, because pharmacology is a dynamic field in which important changes may and do occur rapidly; it would not work because compulsive restriction to standards leads to defeated initiative and stultified thinking.

The obvious approaches to discriminate selection of drugs would appear to be to develop and keep alive an up-to-date standardization of basic clinical pharmacology as the keystone of drug therapy; and to enhance closer professional working relationships among the pharmacist, the physician, and the dentist.

Trend Toward Objectivity

One of the earliest, if not the earliest, organized programs which aimed at collaboration with the physician in the objective selection of drug agents was conceived in 1927 in Syracuse, N. Y. Dr. M. S. Dooley, then director of the department of pharmacology of the Syracuse University College of Medicine, and now emeritus professor, inspired and guided in that early pioneering action to clear up what was a chaotic situation.

Dr. Dooley's plan was set in motion at Syracuse University Hospital in 1932 when the idea of hospital pharmacy practice in association with a pharmacy committee was relatively new. As time passed, more hospitals adopted the idea until today it is accepted by many institutions as an integral part of their professional operations. A significant portion of the historic 1937 "Report of the Committee on Pharmacy" of the American Hospital Association was related to the experience at Syracuse in improving the whole field of drug therapy.

A similar reorganization plan of drug therapy procedure was instituted in the early thirties at New York Hospital in Cornell University Medical Center, New York, N. Y. Publication of their therapeutic conferences in the *Journal of the American Medical Association* and in book form has contributed much to the literature on this subject.

Handbook of Drug Therapy

Late in 1948, the Division of Hospitals in the Public Health Service Bureau of Medical Services initiated the preparation of a handbook which would embody primarily the principles of a sound but flexible system of drug therapy in the 18 hospitals and 22 out-patient clinics now administered by the division. The final handbook would in no way be limited to a list of items in the manner of the traditional formulary. The goal was improved therapy—a goal to be accomplished by cooperative effort which would discredit any implications of interference with personal prerogative.

Thirty-four Public Health Service officers, professionally representing medicine, dentistry, and pharmacy, contributed to the finished text of the new handbook, "Basic Drugs: U. S. Public Health Service Hospitals and Clinics." The pharmacy committee at the Public Health Service out-patient clinic in Washington, D. C., spearheaded the project with close support from the pharmacy committees of the Public Health Service Hospital in Baltimore, Md., and of other Service hospitals. Also, authorities in a number of leading universities and teaching hospitals were consulted.

The main objective of the study was to select the best, the simplest, the fewest, and the safest medicines currently needed in the prevention, diagnosis, and treatment of illnesses. In accomplishing this, the chief task often was one of eliminating duplication and overlapping of items rather than that of sorting out the good from the bad or indifferent. This was a difficult and time-consuming process, especially when it sometimes involved, as it did, giving up a favorite drug which had been successfully utilized over a period of years. As expected, most of the difficulties arose in those areas where fundamental knowledge was not truly adequate and where differing views were advanced by the "experts." In certain of such areas, the drugs selected represent compromises.

Selection Criteria

The following criteria were utilized in the selection of drugs for the handbook:

1. The primary criterion was therapeutic efficacy. Within this criterion, preference was given to items listed in "United States Pharmacopeia," "National Formulary," "New and Nonofficial Remedies," and "Accepted Dental Remedies."
2. Unnecessary duplication was avoided.
3. Drugs of secret composition were not considered.
4. Mixtures were included only when they provided substantial advantage over the individual components.

Barbiturates: An Example

In considering the scope of drugs to be selected, attention was given to the drugs representative of the various pharmacologic or therapeutic groupings and the clinical needs to be met.

Typical of the selection process is the sequence of activities which led to the choice of certain barbiturates as basic hypnotics and sedatives:

1. The barbiturates, as a class, were compared with other U.S.P., N.F., N.N.R., and A.D.R. hypnotics and sedatives. It seemed clear that for general usefulness, the barbiturates represent the surest, simplest, and safest of the hypnotic and sedative drugs. Their range of usefulness extends from mild sedation through spasmolysis and hypnosis to general anesthesia. The therapeutic range of safety is relatively great, most of the unfortunate sequelae being deliberate rather than accidental.
2. Since the nature and degree of effect are largely a function of dosage, the truly basic differences which exist within this class relate to the rate at which they are rendered inactive in the body. This, in turn, affects their duration of action. From the standpoint of therapeutic need, clinicians agreed on four ranges of action: Short, intermediate, long, and ultra-short (anesthetic).
3. Selection of the best agents to meet these needs became the next stage in the process. After much deliberation over the qualities, reliability, official status, usage experience and related aspects, the choices in the short and long ranges were secobarbital and phenobarbital, respectively. Thiopental was the obvious choice for the ultra-short representative. However, most of the discussion centered upon the selection of a barbiturate of intermediate duration of action. After the pharmacy committee discussion narrowed the field to two drugs, the opinions of specialists and consultants were requested. It became clear that custom had been the determining factor in most instances. Since the balance in terms of familiarity of usage and in certain aspects of consistency of action seemed to favor pentobarbital, it was selected as the basic barbiturate for intermediate duration of action.
4. The next step was to prepare the material on this subject for incorporation into the manual. The pharmaceutical, chemical, pharmacologic, toxicological, and dosage information considered essential to the clinician, pharmacist, and nurse were prepared and presented to the pharmacy committee for comment, criticism, and suggestions. When a draft had been agreed upon, it was duplicated and given to the staff as a trial guide, and the pharmacy stocks were adjusted in line with the agreement. After a brief trial period of several months had shown that therapeutic needs were adequately met, the material was made available for joint consideration with the pharmacy committee of the Public Health Service Hospital in Baltimore. Subsequent to agreement with that committee, the material, along with the remainder of the manual, was sent to each major clinical facility of the

Public Health Service, and to national authorities, for their consideration.

5. The suggestions and criticism resulting from these reviews were integrated into the final product. This, in turn, was carefully scrutinized by the headquarters staff with especial reference to the actions which had been taken on the comments and suggestions received from the field stations.

Thus, in the processing of the material and the selection of the basic drugs in the class of barbiturates, as well as in all other classes, most of the clinicians in the Public Health Service have had an opportunity to have their views receive appropriate consideration. Hence, the end product truly represents one achieved by joint action and agreement.

At some future time, a significant number of physicians may find that one of these barbiturates doesn't meet normal expectations. That kind of opinion usually has meaning because it is formed from adequate, first-hand observation. It is an opinion which cannot be formed easily or reliably when a large number of like drugs are used without regard to relative advantage and the unnecessary duplication which may exist. It gives the pharmacy committee and the clinician a basis for reevaluating the drug, perhaps leading them to seek a replacement, or possibly a supplementary drug. They may find that the agent in question, despite its shortcomings, should be retained because it is the best available drug for the purposes required. Thus, the whole approach is kept as scientific, objective, and independent as this field permits.

The Scope of Basic Drugs

The treatment given the barbiturate group is illustrative of the other groups. The items finally selected then form the basis for the pharmacy supply of drugs and drug preparations. Except for nonbasic drugs temporarily stocked for investigational or other special committee-authorized purposes, the drug supply consists of the basic agents.

The field of drug therapy being what it is, additions or deletions are to be expected, and the clinician is encouraged to propose changes. A request for an addition is placed on the agenda for a forthcoming pharmacy committee meeting. When the prescriber finds it necessary to use the drug before the scheduled committee discussion, a small supply is obtained for the particular patient if none of the available basic drugs is found adequate and if there is no immediate, serious objection to the proposed drug. At the meeting, the clinician requesting the drug presents the reasons for wishing to use it. After a general discussion, the pharmacy committee may vote for acceptance, denial, or a trial period of tentative acceptance.

This procedure does several things:

It maintains freedom of action for the prescriber within the framework of the scope of basic drugs.

The prescriber is encouraged to think through the reasons for wishing to add drugs or to drop previously accepted ones. If a proposal cannot stand on its merits in a free discussion among colleagues, there should be little regret about its demise.

The pharmacist, as a committee member and consultant in drug therapy matters, is given greater opportunity to apply his professional competency.

The adopted coverage, as presented in the new handbook, provides a standard of comparison for the evaluation of new therapeutic agents.

Finally, the adoption of a basic range of therapeutic agents and the procedure for going beyond it help provide the patient with the best in the way of established drug therapy.

Two examples may serve to illustrate the validity of this approach:

Surgeons have need for a safe, reliable, orally effective relaxant of skeletal muscle. A new drug reputed to have such effect was proposed for trial on certain patients selected with the cooperation of the chief of the surgical service. Disappointing results were reported about a year later to the pharmacy committee with a recommendation against stocking the drug in the pharmacy.

Surgeons also have need for a good sympatholytic agent. Here, too, they tried out the agent of their choice and reported the results. In this instance, however, they were impressed with the value of the drug in selected cases. Their recommendation that it be stocked as a nonbasic drug for such use and for future reevaluation as a possible basic drug was accepted.

Nomenclature

Drug names were another problem in the efforts to devise a procedure for promoting sound

drug therapy. There is the professional and economic problem of multiple drugs and drug preparations which differ in name only. There is also an element of safety to be considered.

Is it not as important to have a standard terminology for drugs as it is to have a standard terminology for names of diseases, for causes of death, and for the anatomy of the body? Accurate communication with respect to drugs is certainly of highest importance here and extends beyond that which exists between physician and pharmacist.

Various texts, devised as aids to medical terminology, have been prepared for the use of medical record librarians. But when it comes to drug names, the medical record librarian has met with frustration. The situation is of even greater concern to the nurse, who has to administer drugs. With these problems in mind, the following principles of drug nomenclature were adopted:

1. Official drugs listed in the "United States Pharmacopeia" or in the "National Formulary" are referred to by their official English titles. Examples are:

   Hydrous wool fat—*not* lanolin.
   Methyl salicylate—*not* wintergreen oil, *nor* gaultheria oil, *nor* betula oil, *nor* sweet birch oil, *nor* teaberry oil.

2. Nonofficial drugs listed in "New and Nonofficial Remedies" of the American Medical Association and in "Accepted Dental Remedies" of the American Dental Association are referred to by the generic, nonrestricted name assigned by the drug councils of the two professional associations. For example, chorionic gonadotropin, the N.N.R. generic name, is used instead of the numerous names listed for this agent.

3. In some instances, an official drug such as naphazoline hydrochloride having the trade name Privine Hydrochloride, or an N.N.R. drug such as lidocaine hydrochloride with the trade name Xylocaine Hydrochloride, is produced by one manufacturer and is obtainable only under the trade name. Such drugs are referred to in the handbook by the official name or by the N.N.R. or A.D.R. name, as the case may be, and are followed by the trade name in parentheses. The trade name is used in hospital prescriptions to avoid ambiguity where orders are given directly to a nurse. It seemed impractical and pedantic to use the official name naphazoline hydrochloride, for example, when the drug is obtainable only as Privine Hydrochloride. It is especially impractical in instances where ampuls bear the label or imprint of the nonofficial name. Often, the drug later becomes available under the official name or under other trade names. Then the previously exclusive trade name is dropped, and a return is made to the common base: the official name or the generic nonofficial name.

By this attention to drug names, it is possible for all concerned—physician, dentist, pharmacist, nurse, medical record librarian—to speak the same language. Moreover, the pharmacist is able to discharge a professional function for which he is trained, that is, the selection of the best drug from the pharmaceutical standpoint. No longer is there need to overload the pharmacy with many brands of the same drug or drug preparation. And as to therapy, the physician need not be concerned with much more than the selection of the therapeutic agent and the dosage. He decides, for instance, that the patient should have aluminum hydroxide gel in stated doses. The pharmacist is free to select the best available product without having to burden the pharmacy with many brands of the same item.

The Pharmacist

The success of a program of sound drug therapy depends in large measure on the professional stature of the pharmacist. To some pharmacists, as to some physicians and dentists, this type of operation may mean a departure from deeply rooted pathways of thought and action, calling for a new perspective on their part in the handling of drugs. It calls for basic knowledge not only of technical pharmaceutical functions but of drug action and drug use as well and of the differences and shortcomings which may exist among drugs. It means an awareness, for example, that witch hazel water, which would not be included in the basic drug scope, is nothing more than alcohol, water, and a witch hazel aroma—that witch hazel water will do little more than will an aqueous, 14- or 15-percent dilution of alcohol. What is most important is the ability to present

this type of information in scientific and, above all, unobtrusive fashion.

In administration of the program, it should be understood that "Basic Drugs" is not an instrument of rigid control but is essentially the sine qua non for maintaining a coordinated approach to sound drug therapy. The prescriber is encouraged at every opportunity to demonstrate his reasons for wishing to add a drug to the basic list and is not refused a drug merely because it does not appear there. The whole objective will fail if the physician or dentist is in any way discouraged from questioning the existing list. On the contrary, they should be encouraged to be analytically critical. This will serve to improve this tool and to sharpen therapeutic acumen. The goal is improved therapy—not disciplinary control.

Several courses of action are open when the pharmacist who receives a request for a nonbasic drug informs the prescriber that the drug is not currently stocked:

The prescriber may ask if a drug of like action is available.

Or the occasion may be such that the pharmacist can take the initiative by suggesting the available analogous drug. The prescriber may decide to use the available drug and then find that it is the equivalent of, or better than, his first choice. Whenever that happens, it is a confirmation of our selection methods.

If there is doubt about the basic drug, the pharmacist may encourage the prescriber to present the drug originally requested to the pharmacy committee for acceptance. If the occasion demands, the pharmacist will offer to secure the nonbasic drug for the patient, subject to approval from the chief of the service, until committee action is taken.

Core of His Activities

After the system is in operation, members of the medical and dental services become familiar with the procedure, and the rest is automatic.

Once the pharmacist is relieved of accumulations of unnecessary drugs, he can then focus his attention on the drugs which he knows represent the core of his activities. He is free to acquire complete knowledge about these drugs and to consider improvements in ways of administering them.

Would this mean less work for the pharmacist? Not necessarily.

Take cough preparations as one example. There are almost as many of these as there are coughers. Under the basic drug approach, the fundamental physiology of coughing was examined and the bases for therapy were determined. Ammonium chloride was selected for its general liquefying and expectorant effect to aid the removal of sputum from the respiratory passages. Codeine was selected to depress the cough reflex when the cough becomes excessive or futile. Finally, potassium iodide, subject to certain contra-indications to its use, was selected for liquefying especially tenacious sputum which has not yielded to other measures. The responsibility for devising suitable vehicles for these agents now resides with the pharmacist whenever their administration is desired in liquid form.

This illustrates a situation calling for additional work by the pharmacist since agents used previously may have been purchased instead of having been prepared in the pharmacy.

The Open-Staff Hospital

How does a system of sound drug therapy operate in an open-staff hospital?

Usually the approved scope of drugs, previously agreed upon by the chiefs of each service in collaboration with the pharmacy committee, is used as the basis for drug therapy on ward service. It is understood that only the basic drugs are stocked in the hospital pharmacy. Nonbasic drugs prescribed for private patients are purchased (for the patient and not for "stock") without delay and in the minimum available quantity. In time, physicians who attend on ward service are able to evaluate the basic drugs used, and, once assured of their soundness, usually employ the same drugs for their private patients. Soon there is a diminishing number of special purchases of nonbasic drugs except for those under investigation.

The critical factors involved in the operation of the system in such hospitals are these: the need for prior agreement on the part of the chiefs of each service; the selection of a physician as guiding hand in the program who is aware of the problems to be tackled and the

objectives to be achieved; and the collaboration of a pharmacist with the same awareness.

Drug Manufacturers

It should be understood that a program of sound drug therapy is directed toward a logical application of drugs in the treatment of illness. The pharmaceutical manufacturer serves an indispensable function in accomplishing that aim. Manufacturers who inquire about the new program are admittedly interested in its effect on their operations, but they are soon convinced that our interest in having an opportunity to assess the new, that is, really new and potentially effective therapeutic agents, equals their interest in bringing the new drugs to our attention. As in all competitive enterprise, here too there is just as much chance for the manufacturer to gain as to lose. Proposed drugs are given every consideration. A drug which is finally adopted after organized, careful scrutiny has the substance and the chance of survival that otherwise may not obtain.

Conclusion

Thus, an attempt has been made to keep the base—the point of departure—not the end, but the means to the end of the soundest drug therapy available at this time. The degree to which this is successful depends on an appreciation of pharmacology as the basis for sound therapy, of the need to keep the base alive and up-to-date, and of the need for professional coordination of the fields of pharmacy, medicine, and dentistry.

The purpose of the foregoing has been to enunciate a principle of operation which has been found useful, but not to stipulate either method or content in detail. The circumstances brought about by certain existing confusion in the field of drug therapy led to the development of method and content designed to meet particular Public Health Service needs, but it is believed that the underlying principle of this approach is broadly applicable.

REFERENCES

(*1*) 422 new pharmaceutical products launched last year, survey shows. Reported figures revised according to personal communication from Paul deHaen. Drug Trade News **27**: 26 (April 28, 1952).

(*2*) U. S. Public Health Service: Basic drugs: U. S. Public Health Service hospitals and clinics. Washington, D. C., U. S. Government Printing Office. To be published.

Children's Bureau Appointments

The appointment of Elizabeth Healy Ross, M.S.W., to the newly created post of deputy chief of the Children's Bureau and of Melvin Glasser, B.S.S., as special assistant for State and national organization relations on the bureau's juvenile delinquency project, was announced in September by the Federal Security Administrator.

Before coming to the Children's Bureau, Mrs. Ross, a psychiatric social worker, served as consultant to various Federal and District of Columbia agencies, including the National Institute of Mental Health. A member of both the American Association of Social Work and of the American Association of Psychiatric Social Workers, Mrs. Ross was elected a member of the executive committee of the National Conference of Social Work in 1951. She is a member also of the panel on Mental Health of the President's Commission on Health Needs of the Nation.

Mr. Glasser was executive director of the Midcentury White House Conference.