Medicinal chemists have done wonderfully with the efficacy. They need now to do something about the second parameter—safety.

If medicinal chemistry is to fulfill its mission it needs to work closely with the biologists in particular, with the pharmacologists and toxicologists, and to develop more meaningful ways of assessing the potential of a new pharmacodynamic before bringing it into the clinic. New and imaginative approaches are essential, and this can only be obtained by an even greater involvement of medicinal chemists in the experimental work in animals.

The time has come to include toxicity and side effects in our textbooks dealing with chemical structures and therapeutic activities. We should begin to correlate data collected over the years and begin to treat these data much in the same way we are treating biological activity. Let us use our computers and every sophisticated tool at our disposal to expand our capacity to predict animal efficacy and toxicity in terms of man. It is timely to begin learning the relationship between the way different species metabolize a drug in terms of the parameters efficacy and toxicity. We must learn how to correlate these data with the behavior of the drug in man. Perhaps we shall begin to know why drugs may be ineffective or toxic to a few patients but not to most and why individuals handle drugs differently. If we can build up a store of knowledge in pharmacogenetics, perhaps we shall be able to predict which patient should or should not be treated with a particular drug. In short, we must learn to know how different patterns of metabolism dictate the usefulness of a drug.

This is the way I view what medicinal chemistry will need in the years ahead, but, as I say this, I realize that scarcely any two discoveries have been made in the same way. As we go down the list of morphine, insulin, sulfa drugs, antibiotics, steroids, and psychopharmacological drugs, what impresses me most is the ingenuity of man. I believe that this power of the human mind will overcome the obstacles we see in our paths today. There are many, great holes in the physician's armamentarium, and we have the capacity to fill them. This is the challenge on which depends the future not just of medicinal chemistry as a science but, more importantly, of drug discovery and development.

Primary Transmission of Scientific Information—Today and Tomorrow*

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The question of content of medicinal chemical journals is discussed. Medicinal chemists require information from clinical, health science, pharmaceutical science, and chemical science areas to carry out their work. Changes which may occur in journals in the future are considered.

Decisions in economic areas—e.g., printing costs *vs.* methods, subscription rates, and page charges—are relatively easy in comparison to the question of journal content. Alfred Burger has said that he does not want the *Journal of Medicinal Chemistry* to be a journal of second rate organic chemistry. I know that all of us agree with this and are glad that he had the courage and will to make it much more than that. But what then should be the content of the Journal?

The primary transmission of scientific information is of crucial importance in all aspects of the process of the preparation of new drugs. It is clearly of importance in the planning stages of this work, and it may not be overstating the point to say that prior information, taken together with individual creativity, are the two most important factors in the design of new drugs. In some fields, the primary scientific information required for the planning of a new project may encompass a limited scope. Individuals who work in such fields, therefore, have a relatively simple task in selecting the journals necessary to satisfy their informational needs. All of us here are aware that this is not the case in medicinal chemistry.

The medicinal chemist must have information from four broad areas even to be able to plan a project in medicinal chemistry. He must, in the first place, have information from the clinical area, because the design of a new drug is clearly a response to a clinical problem. He must, secondly, have information from the area of the basic health sciences—physiology, pharmacology, biochemistry, pathology, microbiology, and biophysics. This information is required for the chemist to understand the clincal problem in molecular terms. In a few cases, we may even have a fairly good idea of the molecular processes underlying a disease state. However, this is usually not the case. More often, we have some scattered information on the physiology and biochemical basis of a disease state and must make assumptions concerning the rest. In any case, the rational design of new drug entities requires the full application of all the basic health sciences to the problem at hand.

Thirdly, the medicinal chemist requires information from the pharmaceutical sciences. It is now well known that the type of dosage form may markedly influence blood levels of a therapeutic agent. The type of tablet employed in an oral form, or the type of vehicle utilized in a topical preparation, may influence the activity of a substance to the point of causing an active compound to give a negative result in a biological test. This rapidly expanding area, therefore, is one which must be understandable to the medicinal chemist in the course of his design studies.

Finally, the medicinal chemist must have the traditional

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information well known to all of us from the chemical sciences. Many of us are trained primarily as chemists and tend to emphasize this aspect of our science. The relative failure in progress in medicinal chemistry at the present time, or perhaps I should say the plateau on which we now seem to be, may well reflect a failure to recognize properly the other three areas in connection with the planning of a problem in medicinal chemistry.

After a project has been planned, it must be executed. Here again, the medicinal chemist must make use of all of the preceding areas in his work. Even during the execution stage of scientific work, continuous revision of strategy is required, so that the planning extends into the actual work itself.

Lastly, after the work has been completed, it must be reported. Here the medicinal chemist faces a real dilemma. In the past, many medicinal chemists have reported the chemical aspects of their work in the chemical journals and the biological results in the pharmacological literature. With the rise of the *Journal of Medicinal Chemistry,* under the leadership of Alfred Burger, this situation was improved because it brought, for the first time, a major journal devoted exclusively to the combined presentation of chemical and biological data. To the extent that medicinal chemical literature is represented by the synthesis of new chemical entities and the testing of them in conventional pharmacological systems, the *Journal of Medicinal Chemistry* has been successful in bringing about a forum available for this specialized purpose. However, many of us would agree that this limited concept of medicinal chemistry does not represent the full scope of activities important to it in any sense. Medicinal chemistry includes problems in several large areas at the interface of chemistry and biology. For example, it includes problems in the metabolism of drugs in the interaction of biopolymers with small molecules, and in the selective design of inhibitors of enzymatic processes. In short, medicinal chemistry as we know it today, incorporates many of the elements of molecular biology as applied to areas of importance to drug action. The result of this situation is that the scope of the specialized medicinal-chemical journals is narrower than the interest of their readers.

How can we get some indication of the true scope of interest of the readers of the *Journal of Medicinal Chemistry* other than to make uneducated guesses in this direction? An interesting approach to this problem was made by David Gushee in 1970 when he was Publications Manager of the American Chemical Society. He obtained a computer analysis indicating the combination of journals purchased by the members of the American Chemical Society. There are relatively few members who subscribe only to the *Journal of Medicinal Chemistry*—most subscribers subscribe to other journals as well, indicating that their scope of interest is, indeed, broader than the coverage of the Journal. The most frequently subscribed-to journals in combination with the *Journal of Medicinal Chemistry* are the *Journal of Organic Chemistry* and the *Journal of American Chemical Society,* indicating again that the interest of the readers of the *Journal of Medicinal Chemistry* in organic chemistry as such is very high. Other journals which are of interest to these readers are *Biochemistry* and *Analytical Chemistry.* Of course this particular computer analysis was done only on the basis of ACS journals. It would be much more interesting to know what the journal interest of *Journal of Medicinal Chemistry* readers are generally. This could be used as a rational means of journal planning.

What can we anticipate for the future? Medicinal chemistry, like most scientific disciplines, has grown from a small, informal subdiscipline, through the stage of a viable and productive group in which more and more people declared a need for the collection of its ideas and data in a single forum. The result was the *Journal of Medicinal Chemistry.* But it is likely that as the number of medicinal chemists grow, subgroups will develop again, which will meet as small, informal subdisciplines. The question, then, is how these subgroups may best he served by the *Journal of Medicinal Chemistry.*

For the immediate future, we may try to continue to broaden the biological scope of the Journal and possibly to encourage the use of review articles, the new compounds section, abstract section, and the like to cover some of the other areas of interest to readers in medicinal chemistry. For the intermediate future, the *Single Article Service,* pioneered by the ACS Publications Division, may be of interest. In this service, the tables of contents of the Society's research journals are reproduced and distributed to subscribers. The recipients can order reprints of any articles listed. This single article availability is a means of putting a more selective and relevant set of documents into the users' hands. The *Single Article Service* subject-clustering patterns can also be used as a guide for repackaging ACS journals into more selective groupings.

At some point in the distant future, there will be a comprehensive network for scientific and technical information with many avenues of access. In response to user needs, primary information will continue to be disseminated on a routine basis, with the package selectively prepared for individuals or well-defined small groups as opposed to the current tradition-oriented systems. Studies show that users often want only parts of articles, books, and reviews. Such literature will have to be organized and indexed to make accessible in piece-meal fashion.

All of us are familiar with the industrial internal abstract services. The industrial scientist often reads an abstract and secures a photocopy of the article from his library. This sort of system has some of the elements of the one I have discussed. The day is coming when the scientific journal, in its present form, will be thought of as the horse and buggy of scientific information.