

"A program by which the German strangle-hold is to be loosened from the throat of the American dye industry" was made public by Mr. Palmer on that date in an announcement of the creation of an American corporation to take over all the German dye patents and hold them as a trust for the benefit of the native industry. The plan is thus described: "The corporation, to be known as the Chemical Corporation, is non-commercial in character and already owns 4,500 of the *product patents* through which the Germans at one time practically controlled the manufacture of dyes in this country and wholly controlled the importation of them by European concerns which were not German. The Chemical Foundation will hold the patents for the various terms for which they were originally issued and by the granting of licenses under them within devote them 'to the Americanization of such institutions as may be affected thereby, and to the exclusion or elimination of alien interests hostile or detrimental to the said industries, and to the advancement of chemical and allied science and industry in the United States.'"

It is to be hoped that the Chemical Foundation will reform the abuse of the United States patent and trade-mark laws, especially in relation to new medicinal chemicals. New *materia medica* products should not be introduced by advertising. Their manufacture and sale should not be monopolized. They should be open to competition and introduced to science through the medium of the professional societies and press. Advertising should be confined to brands of products, presented to the medical and pharmaceutical professions through the medium of the advertising columns of the medical and pharmaceutical journals. Protection to brands by the proper use of process patents and by the employment of brand names, registered as trade-marks, may not be objectionable, but "product patents" whereby the sale of the products is monopolized by individuals, firms or corporations, hinders progress in science and commerce, discourages improvements in processes of manufacture, protects a system of therapeutic advertising, misleading in character, and therefore the entire patent and trade-mark system as thus conducted is inimical to the public welfare.

It is not my intent to discourage original research. The plan would be ideal if placed on an altruistic basis.

CHEMISTRY'S OPPORTUNITY IN PHARMACEUTICAL RESEARCH.*

BY GEORGE D. BEAL.

Professor Charles H. Herty, Editor of the *Journal of Industrial and Engineering Chemistry* of the American Chemical Society, has recently presented the question of a needed development of facilities for research on medicinal agents as applied to pharmaceutical chemistry. In the editorial column of that Journal for September last he relates a conversation with a chemist who has been prominent in working out methods for the manufacture of coal-tar medicinals. The question is asked, "Suppose during your researches you made some new compound which you believed would prove more efficacious against certain diseases than any of the known compounds whose details of manufacture you have solved, where would you turn to have it tested thoroughly?" And the reply, also quoted, was "I don't know."

* Read at the One Hundredth meeting of the Chicago Branch, A. Ph. A., February 21, 1919.

Few editorials in the journals of that society have brought out the number of comments which have been provoked by those paragraphs. The New York Section arranged a symposium on the subject to which representatives of all of the allied groups contributed. A number of timely suggestions were made as to the manner in which such a need might be satisfied. These included the establishment of a research institute, the endowment of fellowships, the creation of research funds, etc. The chemical society has been so impressed that its Board of Directors has appointed a committee to analyze the situation.

The inference is drawn in the editorial that this country is without such resources, and that if the American Chemical Society does not come to the rescue as the sole accredited body of scientists in the country capable of solving such problems we will be unable to develop them. Questions similar to this have occurred to those of us who have given thought to the development of research touching on the scientific aspects of pharmacy. Probably, however, we have felt that the profession itself was in a position to take care of the problems as they presented themselves. At least we have felt that there was some latent appreciation of the opportunities in the field. Perhaps the spirit of research has not been sleeping so soundly as it has appeared to the members of the allied sciences.

A mistaken point of view is prevalent among the chemists to-day. There is a tendency to belittle all claims of pharmacy to a place among the scientific professions. This is due to a failure to inquire into and to understand the nature of the different organizations of pharmacists. Since the average person's contact with what he knows as pharmacy is over the counter of a drug store, he regards the pharmacist as a tradesman or artisan. He is likely to assume that scientific knowledge of the dispensing of medicines is only required of the man who writes the prescription. When talking of pharmaceutical chemistry, all emphasis is placed on the chemistry, pharmacy representing merely the channel through which the products reach the public.

This idea is present in the mind not alone of the laboratory chemist. Not two weeks ago a member of the Chemistry Committee of the National Research Council expressed the opinion that the American Pharmaceutical Association did not need and had no claims to representation on that committee. He stated in very plain terms that no trade organization need expect to be admitted, that the Council had as its purpose the promotion of research, and that only those who were directly interested in the development of the research idea need hope for admission. The writer took great pleasure in exhibiting the honorable record of the American Pharmaceutical Association and had the satisfaction of hearing him admit his misconception and say that the Association was clearly entitled to representation thereon.

The American Pharmaceutical Association has been a medium for the promulgation of new knowledge and the development of the research idea for nearly seventy years, practically three decades before the American Chemical Society came into being. After reading the early volumes of Proceedings one usually concludes that the American Pharmaceutical Association was the forerunner of this other society, and that the latter came into being only when the field of chemistry in this country had finally developed beyond the stage of medicinal chemicals. There are certain journals published in this country whose pages for even a longer time

have been monuments to the untiring zeal of the pharmaceutical investigator. Botany as well as chemistry has profited by the versatility of those men whose names head the pharmaceutical roll of honor.

This Association has for a number of years recognized the need for steadfast encouragement of the spirit of investigation by the creation and continuance of its research committee. The Division of Pharmaceutical Chemistry of the American Chemical Society has endeavored to support this idea, in part through its Committee on Analytical Methods, organized with a similar end in view.

The University of Wisconsin has taken one of the most noteworthy steps in this direction by securing from the state legislature an appropriation for the establishment at the University of a Pharmaceutical Experiment Station. There under the able direction of Prof. Edward Kremers many valuable results have already been obtained in the development of the pharmaceutical resources of the state. We may mention particularly those studies in the cultivation and marketing of medicinal plants and those leading towards the extension of the volatile oil industry to embrace those oil-bearing herbs which may be profitably grown in that state.

Many people have the idea, as Professor Herty may, that research in drugs must of necessity content itself with the proving and standardization of new remedial agents. The question as to whether or not too much stress is laid on the development of new remedies, and whether the liberal use of an editorial blue pencil on to-day's materia medica lists, particularly of the synthetics, might not result in decided benefits, is at least debatable. We can afford for a time to do with less of such advancement and make a greater effort to determine with accuracy the properties and the underlying reasons for those properties of the many agents which are already known. Such a study will prove the truth or falsity of the claims made for certain vegetable drugs and synthetics, clarifying the materia medica to that extent. This will make for the more efficient use of synthetic and phyto-chemistry and should cause a greater development of organo-therapy.

The past war has developed the latent chemical resources of this country and its people to a remarkable extent, and much of the energy expended in the development of chemical warfare materials, particularly the toxic agencies of combat, can be rapidly turned into the field of synthetic medicine. I feel that we shall have lost one of the material benefits of this war if we do not succeed in making some real use of this talent in the permanent advancement of pharmaceutical knowledge. The average chemist of research caliber is ready and willing to deal with any question of real necessity. In order to avoid duplication and to secure the selection of really desirable fields of work, some agency is advisable from which the general line may be indicated. The writer is of the opinion that some sort of a centralized research bureau should be instituted, in fact, it is becoming necessary if we are to utilize to the greatest extent the resources mentioned.

It has been proposed by a number of writers and speakers that there be established in connection with one of our universities a research institution similar to the Mellon Institute of Industrial Research at the University of Pittsburgh, organized by the late Robert Kennedy Duncan. Such an institution must be endowed as to building, equipment and general administrative and operative staff. It will be possible to refer problems necessary of immediate solution to

the general scientific staff for their study. These will involve pharmacological testing, development of methods of analysis, improvement of manipulatory methods in the plant, the suggestion of new sources of material and the development of new commercial avenues for old products and by-products. In short, such an institute would do for the profession generally what the research and control laboratories of our large corporations do for those organizations.

It is hoped that fellowships will be generously endowed in part for the study of specific problems in which the donors have an interest and in part for study of a graduate order for the advancement of pure science. Nominations to these fellowships would undoubtedly be made by the universities; election ought to be by the governing board of the institution for it appears that they would be the only authority in a position to compare the qualifications of all of the nominees.

In order to be of maximum service the organization must be placed upon an extremely broad footing with the greatest liberality in its field of operations. There is always the danger that an institution which draws its support from the industries may be forced by financial circumstances to devote its time to these industrial problems, in such a way that the spirit of research may become stunted or even choked altogether in its growth and the institution fail in the accomplishment of its purpose. But if in establishing fellowships as liberal action is taken as has been done with the duPont Fellowships instituted in our leading schools during the past year, I believe that the foundation would be in a fair way to accomplish all that it has set out to accomplish.

In order to provide for the greatest possible growth it seems that it would be desirable to secure the establishment at first of a foundation rather than an institute. In the latter case there must be a large initial outlay for the physical plant, administration and operation, and unless such a plant is provided for by outright gift, the capital required in the way of endowment would undoubtedly prevent for some time the commencement of the project. If the work be begun by a foundation, on the interest of a sum held in trust by certain trustees administering the foundation, the establishment of some fellowships is assured and investigational work can be begun by one man in any university laboratory. This plan is not the one which has seemed to be popular, and would not result in the immediate provision of the laboratory resources called for in the editorial which suggested this paper. It will serve as a real working basis and is capable of unlimited development. By all means, let us have our research institute, with its laboratory facilities and research staff available for the assistance of all investigators in the field, but let this laboratory be a natural growth from the foundation, and do not let its coming at first absorb all of the strength which might go towards the promotion of study in the laboratories of nearly every state in the Union.

I have mentioned the need for some sort of centralization of research, some sort of clearing house of ideas, as it were. This is the general policy underlying the National Research Council, which is a child of the National Academy of Sciences. In this council all of the national scientific societies whose object is the advancement of learning are banded together for the prime purpose of preventing lost motion in investigational work. The Council stands ready at all times to suggest lines of study and to advise in the prevention of too much duplication. It will suggest possible avenues of development along which an investiga-

tor may proceed because it is so in touch with the different laboratories that it can provide for the interchange of information and material, for the want of which many an investigation has been abandoned.

To illustrate, the Division of Chemistry and Chemical Technology, one of the nine subdivisions of the Council, during the first year of its existence assigned over one hundred and ten research problems to single chemists or chemical committees in this country. Many of these have been successfully solved because the investigators were able to draw upon all of the facilities for research which their laboratories afforded. The Division has in addition handled many requests for information regarding manufacturers and sources of material used in the industries and in research, has brought about coöperation between investigators on allied problems, has directed the attention of manufacturers to investigations related to their field, and has acted generally as a central clearing house of information.

It should be possible to have in pharmacy a central body in possession of much information of value to any worker; able to procure necessary literature, to secure the coöperation between the manufacturer with an abundance of material and the investigator having behind him only the frequently limited resources of school laboratories. An institution of this kind could be represented directly in the various fields by its own agents, or by the agents of corporations which would ultimately benefit by the development of those new resources. A wealth of material for investigations would speedily become available to any laboratory, no matter how meager its funds for research.

There is difficulty in the testing of new medicinal agents unless the discoverer has the proper pharmacological training. If one is associated in a university with a skilled technician the resources of his laboratory are usually available. With a certain amount of training and supervision the chemist himself can acquire the necessary manipulative skill and ability to interpret results in a rather limited field. But as the chemist and pharmacologist grow in experience and gain a reputation in their fields they usually make for themselves a position of responsibility in their faculty circle. This results in extended duties, administrative tasks, advisory work with students, the direction of large laboratories and courses and a rapidly extending relationship to the whole institution. Unless the investigator be a very exceptional person, the opportunity of continuing his personal investigations has gone glimmering. He must take on research students, divide his problems among them, and content himself with brief conferences and rapid perusals of reports, and the wheel begins another revolution with these younger men.

The investigator may be connected with some manufacturer or have the fortune to interest some manufacturer in his work. In order to secure aid of this latter sort there is necessarily some sort of agreement regarding the possession of production rights to this and other substances derived therefrom. Such an agreement must be entered into in good faith by both parties in order that there will be, on the one hand, no throttling of research ambitions, and, on the other hand, a genuine recognition of the financial support which is making possible the continuation of the study. The one danger most likely to come to pass is that the

student's time will turn gradually to those lines which are profitable financially with too little attention to the scientific development of the field.

One of the greatest obstacles in the way of the investigator in plant analysis is the difficulty of securing allied species for comparative study. The writer has for several years been engaged in a study of the chemical composition of the plants of the *Rumex* family, especially as a source of medicinal agents of the anthraquinone group. Because of limited resources, even in the State University, it has been necessary to limit the investigation to the rather narrow field of a few members of the family found in the United States. The literature reports a partial analysis of the root of an European variety and the composition of the above ground portion of an African variety. If there happened to be some central body with correspondents in different parts of the globe, it should be possible for an investigator to secure enough of representative samples to make the desired comparative study.

There is room now for coöperative work in plant analysis by which a revision will be made of the compositions as previously published. Lloyd and others have pointed out that by the methods formerly used, the proximate principles previously reported have been largely decomposition products of colloidal principles which were directly the result of vital processes within the tissues. This doubtless explains the difference in physiological effect frequently noted between simple drug preparations and crystalline derivatives and also may explain the failure to coördinate physiological activity in many instances with the result of chemical assays.

Alkaloidal assaying consists chiefly of the application of methods designed to take advantage of the comparatively simple differences in physical properties of these bases and their salts. The "shaking-out" process is based upon the principle of the coefficient of distribution. It has been possible by direct measurement to determine the efficiency of the extraction of each alkaloid, which in the case of a single one in a drug constitutes a quantitative separation. In many plants there are a number of related alkaloids, one of which by a slight variation in structure may have more intense activity. The determinations of this individual in a mixture then will require the recognition of a difference in chemical properties, or the formation of a derivative with such properties, as a basis for its separation. These, as a rule, are not problems of a difficult nature, but require careful attention to detail with many duplicate determinations. They are not likely to be taken up without hearty encouragement and support which will render possible the neglect of other work for the time.

The chemistry of American volatile oils cannot progress much farther until provisions are made by which the investigations can be carried into the field. Here, as in the matter of drug composition, all depends upon the authenticity of the samples. The chemist who can go to the herb plots for his material, or who can carry his still into the woods and take the oil as it comes from the plant, has an immense advantage over the chemist who must obtain his supposedly genuine subject from a New York or Chicago jobber. Some one must pay car fare to the woods, and provide portable apparatus, or must furnish plots and agricultural labor for the herbs.

Two of the most striking recent examples of coöperative research have been the development at the Rockefeller Institute of an important anti-syphilitic and the development by Dakin, Dunham and Daufresne of the line of chlorine containing antiseptics from the hypochlorites under the auspices of the British Medical Research Council and the Herter Laboratories of New York. Here the actual proving of the value of these compounds was carried out by beneficiaries of the Rockefeller Institute, in hospitals operated by them. I believe there has been no greater triumph of science in the last war than along the line of the alleviation of suffering and the removal of the liability of the frightful after-fatalities of the battlefield, a triumph which can be traced altogether to the strong organization for research.

Probably more efficiency could be shown in the revision of the Pharmacopoeia if in the past there had been possible a carrying over by a central organization of the Committee on Revision with its sub-committees by whom the necessary investigations could have been carried forward simultaneously with the appearance of the various factors necessitating this revision. The collection and correlation of the mass of literature which appears on any important subject in a decade is no small task. While work being continuously carried forward may be invalidated from time to time by findings of the investigator or by other circumstances, there is no lost motion in taking up the scattered threads of the subject and piecing together a new fabric, more durable than the old, and having greater validity because of the errors recognized and overcome.

The Drug Laboratory of the Bureau of Chemistry at Washington has published some valuable papers on the identification and estimation of the newer synthetics, laying stress on those of more common occurrence in headache and cold remedies. At the same time there are being offered in some of the leading universities courses in qualitative organic analysis having to do with the identification of pure compounds and the separation of mixtures. These courses are being offered by men who in many cases have brought long years of training as research chemists to their work. They have developed simple methods of attack by means of which a student of limited experience but with a thorough grounding in the fundamentals of organic chemistry can rapidly solve the composition of complex mixtures. Such students have but one obstacle to contend with, they are unfamiliar with therapeutic properties and cannot associate substances as is done by the chemist who has devoted his time to the medicinal use of synthetics.

The writer is fearful lest the delegation of the promotion of pharmaceutical research to one institution or association not directly allied with pharmacy may result in the defeat of the purpose which its projectors are attempting to achieve. If pharmaceutical research be made a function of the American Medical Association we would expect it to be interpreted in terms of therapeutics; if of the drug manufacturers it would cause the establishment of a laboratory where manufacturing pharmacy in all of its ramifications would be studied on a large scale and where cost accounting might well be the criterion by which all results would be measured. The National Association of Retail Druggists finds its real interest in the problems which affect the profits and losses of the retail trade, while the American Chemical Society would have a tendency to view everything in its chemical phase. Each group will pay only minor attention to the contributory data which

has been laboriously brought together by students in other fields ever since pharmacy first became a science.

No one association, representing one of the contributing sciences, and not having its major interest in the field as a whole, can be expected to make the generous provisions, nor offer the broad-minded administration or direction, which such a foundation requires. I believe most emphatically that if the United States is to have an institute of drug research, it should be all that the name implies, and should be controlled, or at least feel the guiding hand of, that group which will finally be obliged to accept or reject and be governed in every sense by its findings.

There is only one organization in the United States which has the broad foundation necessary and is so organized as to contain within its membership students from every associated field. That organization is the American Pharmaceutical Association. It has already asserted its right to be the promoter of drug research and has done more than any other organization of the country toward this purpose by the creation of its research committee and by the establishment of a fund for its development out of the sole earnings of the Association.

This sum might be made the nucleus for a large fund to be obtained by donation from those most interested in the promotion of pharmaceutical knowledge. Much will depend upon the attitude to be taken by corporation members, but the Association should not look to those alone. The interests of the foundation should be the interests of each member, and an investment in the foundation cannot fail to return dividends to all of those coöperating in its creation. Most institutions must have small beginnings, but if it is the will of the members of the American Pharmaceutical Association that the Association continue to recognize and forward research, their determination will result in an establishment which will remain for all time as a monument to the ideals of the Association.

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THE TACK IN THE TIRE.*

BY W. L. SCOVILLE.

This is the automobile age; an age of speed, of rapid changes, of swift development. Five years ago—just a little more than the space of a college course—the world was at peace. The road was clear and smooth and the weather was fine. Riding was good. Then suddenly just around a curve the German machine viciously struck the Belgian car, telescoped it, and rushed into the French car coupled with a low-powered British. These stood the shock without collapsing, but were driven back until the German machine realized that it, too, was seriously damaged. Then began a struggle for the roadway which lasted four and a quarter years, which developed ways and means of powers, of repairs and of efficiency with startling rapidity. And because men of science, of skill, of thought, and of dexterity set themselves wholeheartedly to the task of clearing the road and making it "safe for democracy" the struggle is now over and the rebuilding is begun.

* Read at the One Hundredth meeting of the Chicago Branch, A. Ph. A., February 21, 1919.