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RESEARCH AND THERAPEUTICS[1]

By Dr. AUSTIN E. SMITH

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DURING the year 1942 nearly one tenth of the entire population became a hospital bed patient. One person entered a hospital in the United States as a patient every two and a half seconds. Surgical operations were performed at a rate of one to each 5.6 seconds and the hospital birth rate exceeded three live babies to the minute.

This represents only a part of the total illness in this country and is, of course, only a fraction of the illness prevalent throughout the world. By the time the war is over such figures when compared to world-wide statistics will be infinitesimal. At the recent National Conference on Planning for War and Post-war Medical Services a number of papers were presented to show post-war medical needs. Obviously the papers could not be specific in details as exact estimates for post-war needs are impossible to determine at this time, but they did give an indication of the future enormous requirements from the drug manufacturers. Will the demands be met entirely by current drugs or will there be available a host of new agents? With American medicine encountering diseases alien to these shores through participation in world-wide health problems and the return of infected troops, new and more effective agents will have to be provided.

At present the drug-manufacturing industry is faced with many problems—two major ones are increasing reductions of certain basic materials and increasing demands for Lend-Lease, armed forces and civilian use. The probable needs in the early post-war period stagger the imagination. As each manufacturer will have to give careful thought to the optimal use of his supplies, there is afforded a good opportu-

[1] Read before the 1943 Annual Convention of the American Drug Manufacturers Association, Chicago, May 3, 1943.

nity to discard old, outmoded and comparatively useless agents. Here is an excuse to bite a hand that offers food with no disastrous results. If these deletions are offset by the introduction of new and truly effective agents there will be nothing lost but much gained. Undoubtedly successful survival and expanded competition after the war will depend largely on the establishment and output of research departments. Recently we were told of a basic list of drugs which will be needed in occupied countries as they are liberated, that the pooled resources of the world will be taxed to the utmost and that the medical profession and medical resources of this country will be called upon increasingly to meet the needs of the world for medical care and medical services. If our own physicians, scientists and educators are sent elsewhere in the world to administer to the ill and to organize health and educational programs, American drugs will be in demand not only because of availability but also because of familiarity.

Research Participation

The degree to which research is dependent on therapeutics and therapeutics on research is undeniably appreciated by the medical, dental and pharmaceutical professions and drug manufacturers. The needs for research and progressive therapeutics are evident. The physician and the drug manufacturer are responsible for the prevention, diagnosis and treatment of disease. Their course of action is equally evident. Circumspective thought must be given to the inadequacy of existing treatments, the development of new ideas, their laboratory and clinical trial, their practical application. If it is the duty of the physician to prevent illness, to supply proper medical care for those who are ill and to encourage medical investigation, is not the drug manufacturer faced with the same responsibility? If the health of a nation depends on medical attention, does it not also depend largely on those who supply part of the treatment? And if the medical profession on the firing line needs assistance, should it not be able to turn freely and expectantly to those in the advance supply line?

Often one is asked who should take the initiative in drug research, the physician or the manufacturer. The answer is simple: Every one capable of doing meritorious work should participate. No one will wait for his neighbor if there is sufficient interest in the project. This has been especially true in the last decade and will continue after the war. During normal times research provokes increased business and better health. During times of war it is a patriotic duty to increase research activity; new agents are needed; faster methods of manufacture are essential; better storage conditions are helpful. In the top-notch center such responsibility is shared by all participants as they are interested not only in progress in their respective fields but in survival of their own places in these fields.

There is more to research than developing a new extract or a synthetic compound. The new agent must be carefully studied in test-tubes, on bacteria or animals and in the human. Such studies are complete only when proper working facilities are provided. If the manufacturer has not the space, equipment or trained personnel, the work can be completed elsewhere. When there is joint research the drug house and the investigating physician have certain responsibilities to each other: these should be clear-cut and well understood before any action is begun; otherwise friction and discontent will develop.

Progress in therapeutics does not depend entirely on the development of startling new drugs. Contributions may be offered through studies on diets, atmosphere, clothing, habits; in fact anything which will aid in the prevention and treatment of illness and increasing life expectancy is worthwhile. Too often improperly trained or equipped groups spend prohibitive amounts of time and money searching for miracle agents which are beyond their scope and overlook something practical close at hand.

Changes in Therapeutics

There are many who fail to realize how much progress has been made in the last twenty years in materia medica. In a certain book published in 1899 may be found ingredients of compounds commonly used at that time. One "uterine tonic and restorative" contained unicorn root, catnip, cramp bark, mitchella, cohosh, cinnamon, orange peel, caraway, sugar, diluted alcohol and water. How much different was this formula from those used by civilizations many centuries older! While many such mixtures are still evident they are fairly rapidly disappearing, largely because of the demands of science and of the spirit of competition. In fact, how often to-day do we hear the term "uterine tonic and restorative." A "neuralgic pill" consisted of extract of hyoscyamus, extract of conium, extract of Ignatia bean, extract of opium, extract of aconite, extract of cannabis indica, extract of stramonium and extract of belladonna. A treatment for diarrhea and dysentery offered blackberry root, galls, cinnamon, cloves, mace, ginger, blackberry juice, simple syrup, glycerin and diluted alcohol. Remedies for "female disorders," asthma, baldness and "blood purifiers" contained no end of ingredients. Such mixtures were frequently used less than forty years ago, even though the treatment of disease is

almost as old as man. It takes no trained eye to scan scientific literature and perceive that therapeutics has progressed by leaps and bounds in the last twenty years. Such progress has been born directly of research. Were it not for research the world would still be lacking serums and vaccines, sedatives, anesthetics, vitamins, anti-infective agents and countless other agents. Were it not for research there would be no high-caliber medical, chemical and other meetings, nor would there be the galaxy of published papers now at our command.

Expediting Research

Unquestionably there are delays in research and therapeutic advances—one of the greatest contributing factors is probably misunderstanding: misunderstanding by the physician, educational or research center and manufacturing directors of what a drug manufacturer is capable of doing; misunderstanding of what may be expected of and by an investigating clinician, chemist or pharmacologist or other scientist; and misunderstanding of what may be expected of and by a research center. Such misunderstanding has long served to perpetuate existing confusion, and yet it is surprising to observe how few attempt to ascertain and remove the cause of the confusion.

The first step for any proposed investigation is a consideration of the practicality of the problem and an outline of the program. Then must be determined the limitations of the investigator or the manufacturer. Frequently there is failure to realize existing potentialities and to make the most of these. Of equal frequency is failure to realize one's limitations and the end conclusion is a dismal lack of success or, at the most, uncritical results. Perhaps part of the fault lies in the assigning of incompetent individuals or groups to make the necessary surveys; such incompetence may exist any place along the line of proposed action. Unless the causes for confusion and misunderstanding are removed no individual or organization can hope to contribute the best to the maintenance or promotion of health.

Having decided what can be done, the next decision concerns how it can be done best. Frequently this raises the question of expansion. Expansion, whether it be by a drug manufacturer or by a center of investigation, must be made on a solid foundation. Sometimes expansion is impossible, in which case it is much better economically and otherwise to remain firm and avoid the risk of regression. Too often there is failure to realize that the promoter and investigator are best suited for a particular type of job which could make them outstanding in the one field but which would leave them far behind if they attempted to work in totally alien fields. It is through a proper evaluation of one's scope of activity that we expect to be able to shrug aside such headlines as the following that appeared in a recent trade journal, "German Economic War Purposes Holds World Chemical Control." In view of what has been observed of American drug ingenuity, how can any other nation hold chemical control unless that nation is deliberately permitted to do so? Cheerfully on the same day there appeared an article entitled "Anti-Malarial Ammunition. Synthetic Drugs Will Match Former Quinine Production in Curative Power." When one can speak of the manufacture of billions of tablets of atabrine, tons of vitamins and hundreds of tons of sulfonamides, things which have been developed within a few years, one realizes the tremendous possibilities of research and therapeutics. One has only to look at the statistics provided in bulletins offered by the Department of Commerce and the U. S. Tariff Commission to comprehend the diversity and enormousness of drug manufacture in the United States.

Cooperation

Perhaps the thing which is contributing most to the present stage of development is the close cooperation of various sciences and specialists. Engaged on common problems may be found biochemists, organic chemists, physiologic chemists, pharmacologists, immunologists, clinicians, pharmacists, dentists, etc. Truly no one individual nor any one science stands alone as they may have in the years gone by. Contributions to materia medica have been made by practically all sciences; in no other field is there any closer affiliation between varied interests. In no other field can racial and national differences be more completely forgotten. Undesirable secrecy is disappearing, distrust is showing hopeful signs of receding and ideas are exchanged freely in conferences and at scientific meetings. Daily there are appearing announcements of new drugs, new research, new sources of outlet and agreements with other nations to promote hemispheric trade. Cooperation with adequate evaluation of one's scope plus a fair amount of aggressiveness will provide more drugs, better therapeutic technics and opportunities to partake in the existing agreements and others which will follow. Willingness to cooperate on medical problems not necessarily restricted to this country can be a most forceful weapon in promoting international developments, understanding and good will.

Summary

Progressive therapeutics depends on research, but at the same time it is a marked stimulant for promoting research. Through research will come much of the

post-war advancement which may occur in medicine and allied sciences, drug manufacturing and educational centers. Success and survival will depend not only on cooperation, leadership and a shrewd business sense but on an adequate appreciation of opportunities, limitations and the value of fostering research by providing grants and fellowships. Much material assistance can be provided with mutual gain for all participants when such fellowships are established. This gain may extend past current problems into lifelong associations. If the manufacturer recognizes his opportunities and obligations and forges ahead to challenge or accept them instead of remaining on the defensive, there will be less likelihood of being fettered by purblind policies. Each one interested in research and therapeutics has responsibilities peculiar to himself, but there are few, regardless of occupation, who, at the completion of a job well done, does not feel as Pasteur, who said of the researcher:

> It is indeed a hard task when you believe you have found an important scientific fact and are feverishly anxious to publish it, to constrain yourself for days, weeks, years sometimes, to fight with yourself, to try to ruin your own experiments and only to proclaim your discovery after having exhausted all contrary hypotheses.
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> But when, after so many efforts, you have at last arrived at certainty, your joy is one of the greatest which can be felt by a human soul, and the thought that you will have contributed to the honor of your country renders that joy still deeper.

THE INTRODUCTION OF NEW VIEWPOINTS AND SCIENTIFIC CONCEPTS IN GENERAL BOTANY[1]

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IN any consideration of the approach to be utilized in presenting general botany to students of random selection and average ability, it is obviously necessary to examine with care the general aims of such an offering. It is also necessary, in this transitional period in methodology, to examine critically all current tendencies and evaluate them; one must further correlate the last named with certain recognized, sound and acceptable principles of scientific instruction at the college level. Lastly, it is imperative that we interpret and apply all controversial procedures within the limitations of personnel and equipment of the average undergraduate college.

Work at the college level is not to be confused with that of elementary grades in which the teacher is concerned with immature, plastic minds. Neither is it to be considered as similar to that offered at the secondary-school level, in which we have no selection of students whatsoever other than natural and no aim other than very generally cultural. College botany is a course offered to at least a pseudo-mature student body in which some degree of selection has operated, since only a very small percentage of high-school graduates enter college. At the worst, we are thus facing a selected group of students who should begin to divorce themselves from an immature approach to their studies. The fact that only one per cent. of the students taking general botany continue in the subject for advanced work does not change the last statement to any degree. One cogent, major aim of teaching remains fundamentally the same: a flexible and inspirationally directed assimilation of factual data and principles of proven worth with applications to those life situations within the mental scope and experience of the individual in question; factual data with which to achieve a concurrently developed, intelligent, appreciation with a concomitant curiosity as to plants, their reactions to factors in their environment, and their economic or biotic aspects, *i.e.*, plant sociology.

With these fundamentals, the fad of the moment, the latest tendency (often revived) of the professional pendulum swinger in methods, is simply incorporated into the inescapable and irreducible fundamentals of any science—namely, the assimilation of sufficient data upon which to laminate intelligent concepts; the precursors of a lasting constructive curiosity fostered by satisfaction in mature achievement rather than the immature, rambling questioning of untutored minds. Thus, whether you are striving to develop a sense of citizenship, achieve indefinite sociological aims, or direct a student in the first steps along the road to a professional scientific career, it is here in this freshman course that we must somehow bring him to see the necessity of accumulating data, developing powers of observation, achieving mental discipline, correlating factual agenda with immediate and general environment, and, finally, bring about the development of an inherent appreciation and curiosity

[1] A paper presented at the Symposium on the Teaching of Botany at Dallas in 1941 before the Botanical Society of America and the American Society of Plant Physiologists.