# Fundamental Research in the Clinical Specialties

V. Everett Kinsey

*Howe Laboratory of Ophthalmology, Harvard Medical School, and Massachusetts Eye & Ear Infirmary, Boston*

THE SUCCESSFUL OUTCOME OF GOVernment-supported research during the war has focused the attention of the public as well as professional groups on the desirability of continuing a part of this activity. Bills to provide funds for research in various branches of science are now before Congress. That these bills have not passed perhaps reflects the divergence of opinion of scientists on the details of administering potential funds rather than the temper of the people on the question of public support of research. It seems possible, therefore, that in the future Congress may appropriate funds for general research purposes. Although lack of funds is one of the chief factors limiting additional research, a comprehensive plan by which expansion may be carried out is just as essential as ample financial support.

In order to determine the present status of fundamental research in the clinical specialties and the readiness of clinical laboratories for expansion when more adequate financial support is provided, the writer has visited a number of medical schools. In general, the impression was obtained that research teams adequate to cope with the fundamental problems in clinical medicine are few. This was confirmed by many of the clinical men interviewed, who expressed dissatisfaction with the present lack of teamwork between clinician and scientist in basic research.

Among the points studied particularly in arriving at this conclusion were: (1) the organizational methods by which research is conducted; (2) the magnitude of the research; and (3) the extent to which the needs of the particular clinical specialty are fulfilled.

Only the larger university medical schools were visited, since it might be presumed that fundamental research would be conducted in these universities on as large a scale as anywhere in the United States. The schools were located along the Atlantic Seaboard, in the Middle West, and on the Pacific Coast.

Typical of the conditions discovered is the situation in a clinical department of one of the midwestern universities. The head of this department is well known in his field. Clinical facilities appeared to be excellent, and space is available for making experimental studies. However, since the termination of a large grant five years ago no full-time investigators have been employed. Members of the clinical staff go to the laboratory occasionally and conduct occasional experiments as a part-time activity. No men from departments of basic science, such as bacteriology or biochemistry, have been assigned to work in the department. Plans have been made to obtain a research director who would be expected to devote half time to coordinating studies made in the department, a quarter to private practice (the income from which would comprise a significant fraction of the research budget), and the remaining quarter to work of his own choice.

Another instance which is not typical but which illustrates the consequences of halfway measures is the situation in a department located in a teaching hospital in a large medical school in the East. The department head is a clinician who previously gained an international reputation for his research work. Unlike that of most men in this position, his salary is adequate to allow him to devote full time to the department—in fact, the position was especially created so that he might have more opportunity for institutional activity, particularly for the "luxury" of research. When asked whether, under these apparently favorable circumstances, the research in his department was developing satisfactorily, his unhesitating answer was "no." Although he believed that the provision for full-time academic work was a step in the right direction, he estimated that 90 per cent of his time was taken up with such administrative duties as obtaining new house officers, making rounds, settling petty squabbles, and numerous other details requiring the attention of a department head. Moreover, research by others on the staff is sporadic; an excellent young investigator was recently forced to enter private practice to make a living wage. The only full-time studies being conducted at present are carried out by a single investigator, a chemist.

In the two departments described definite efforts have been made by capable administrators to conduct research programs within the departments, but these have failed in their objective because of lack of funds. In departments in other institutions visited, no fundamental research has been attempted, and no facilities or personnel are available.

A method of conducting research which is being used increasingly is to assign members from departments of basic science to the clinical department or vice versa. Salaries and duties are divided. In a few instances this method has proved successful; more often the complaint is heard that the clinical man is unsympathetic with the choice of problem and that little actual contact exists between the basic scientist and the clinician, who spends most of his time in private practice. A variation of this

arrangement is for the clinician to consult, either by periodic conference or when the occasion arises, with men in the preclinical departments. With the exception of one institution, where periodic conferences were implemented with laboratory work performed by full-time investigators, it was evident that this arrangement produced little more than conferences. The principal weaknesses of the conference method lie in the lack of mutual understanding and time, existence of other interests, and minor annoyances encountered in a joint investigation with busy co-workers frequently located on the other side of town.

Some research in clinical specialties is done in the basic science departments; these researches frequently lack continuity and are often of an analytical nature. As such, they are of great value. However, the mere accumulation of facts is not sufficient; it is important, in addition, *to use them to establish new principles* or to confirm old ones. This is an endeavor which requires background and insight both in the basic sciences and in the clinical field in which known facts are to be used.

In addition to research in medical schools and associated hospitals, an increasing number of studies, particularly in medicine, are being conducted in research institutes and industrial laboratories. Despite obvious limitations, the majority of these are well organized and are performed by trained full-time workers. The clinical testing for both groups must be farmed out to nearby hospitals.

It is impossible to obtain an over-all picture of fundamental research in medicine without taking into account the increased emphasis placed on studying separately such diseases as cancer, tuberculosis, poliomyelitis, arthritis, and those affecting the heart. While these diseases are also the concern of different clinical specialties, they represent single entities, and the study of each is likely to become a specialty.

The number of people working in a given field is small indeed. This is illustrated by an example chosen from the specialty with which the writer is particularly acquainted, namely, ophthalmology. Glaucoma is caused by excessive intraocular pressure, which if untreated, results in blindness through excavation of the optic nerve head. This disease is the chief cause of irrevocable blindness in individuals past middle life and is typical of the dramatic type of illness which might be expected to stimulate research. How many investigators in the United States are devoting half or more of their time to studying glaucoma? Or, more important, how many are investigating basic physiological processes in the eye which might lead to a successful therapy? A generous estimate is *three*.

It is concluded from the information obtained that many halfway measures are being employed in an attempt to carry out research programs in the clinical specialties. As a result, the amount of fundamental research in the clinical field is extremely small in comparison with that in the preclinical sciences. Of the persons interviewed, all but one is dissatisfied with the present state of investigational activities in his field, the exception being a man ready to retire. The implied excuse for this deficient state is a lack of funds available over an extended period. Not only is basic research undeveloped in these fields of medicine, but it is apparent that if sufficient funds to carry out an intensive research program were immediately forthcoming, few departments have any trained personnel or well-laid plans for their effective use. This condition can be attributed in part to a defeatist attitude born of previous unsuccessful attempts to overcome the multiple difficulties inherent in combining an extensive research program with teaching and running a successful clinical department. It seems appropriate, therefore, to consider measures which might remedy this situation.

## Program for Expanding Research

One way to expand research is to increase the number of laboratories investigating specific diseases. The inherent emotional appeal and the ease with which such programs can be delineated are strong tactical arguments in favor of this method. The disadvantages, particularly with small projects which may be forced to advertise their progress, are less apparent but just as real. There is danger, for example, that the interests of research workers may become narrow, that promising leads in the solution of other problems cannot be exploited, and that the feeling of constant pressure to turn up a "cure" may stimulate "long-shot" experiments at the expense of sound but more methodical investigations.

Another means of furthering research in clinical specialties is to establish research institutes in which investigations relating to a number of specialties could be performed. This method offers no appreciable advantage over the one to be recommended and entails considerable duplication of existing facilities and personnel.

A sounder plan, which does not call for significant changes in administration or physical layout, is to establish laboratories staffed with well-trained, full-time workers in the clinical departments of university medical schools. The objective is to develop the fundamental aspects of the clinical specialty and make these available to the postgraduate student. This method is not novel, since it has been successfully carried out over a period of years in the Howe Laboratory of Ophthalmology. Experience gained in this laboratory should be useful in considering a more widespread application of this method.

Historically, there has been little precedent for full-time investigators in clinical specialties; however, the tremendous developments in the basic sciences have suggested many new approaches to the solution of medical problems. These have complicated inordinately the methods of doing research. Whereas in the past many studies leading to fundamental discoveries have been

made by isolated workers devoting their leisure time to research, present-day experience indicates that most progress comes from the cooperative effort of individuals having different training and background. Research of this kind is essentially a full-time job if facilities and personnel are to be utilized efficiently and if the quality of the work is to compare favorably with that in other branches of science.

### The Laboratory for Fundamental Research

The first step in establishing a research laboratory is to secure the services of an able director. At first thought it may appear that the head of the clinical department should also be the director of the research laboratory. This is inadvisable, however, because: (1) directing a laboratory is a full-time job; (2) the person in charge of a clinical department is usually interested chiefly in the practice of medicine rather than in basic research; (3) the head of a clinical department frequently lacks the scientific background which would qualify him to direct research; (4) the clinical professor may be inclined to encourage studies with immediate practical application rather than those of a more fundamental nature; and (5) the demands of his practice would pre-empt both the time and attention of the clinical professor. Actually, both positions are of such importance and involve functions so separate that a parallel rather than a vertical administrative organization is desirable.

The qualifications of the laboratory director should include a sound basic training in either medicine or science, a broad general interest and background in research, and, if possible, administrative experience. It is of greatest importance that the director be wholly in sympathy with the idea of a laboratory in which appropriate problems in basic science are investigated for the purpose of advancing a medical specialty.

A competent staff is no less important for the laboratory. Before selecting a staff it is necessary to recognize that its primary function is to conduct studies of a fundamental nature, not merely to be concerned with case-history reports, statistical studies, and the delineation of techniques.

In recent years advances in clinical medicine have paralleled great developments in the basic sciences. The growth of knowledge in both fields has been so extensive that to become a clinician, a physiologist, or a bacteriologist is a major achievement. Few individuals receive additional training or possess experience outside a single specialty. Accordingly, since the purpose of the research organization is to employ the concepts and techniques of the fundamental sciences in the investigation of problems in clinical medicine, it is essential that the staff include some individuals trained in preclinical sciences and others trained in a clinical specialty.

Each member of the staff should be prepared to conduct independent research and to work on equal terms in cooperative investigations whenever this is to mutual advantage. This type of organization assures that the scope of the work will be more broadly representative of the specialty, permits greater flexibility in the choice of problems, and takes advantage of the combined talents of the staff as a whole. That these talents consist of more than technical skill is not always appreciated. For example, the function of the preclinical scientist in research is frequently assumed to be merely that of a "glorified" technician. This was illustrated recently by the comment of a man who wanted to promote research in his clinical department. He said that what he "really wanted" was a biochemist who could perform analyses, the implication being that the success of a well-developed research program depends exclusively upon the performance of analytical work. In this kind of thinking, emphasis is on the results of analysis and not on the fundamental concepts which are prerequisite to intelligent interpretation. To this man, who is representative of many well-known clinicians of the older school, a person trained in the basic sciences is merely an adjunct to the laboratory whose scientific acumen is disregarded entirely and whose technical services are overrated. In this instance, the mistake is not in obtaining a biochemist but in misunderstanding completely his function in the laboratory. Therefore, to utilize the basic scientist fully it is essential that, in addition to using his technical skill, his intellectual capacities and talents be directed toward the conception and solution of research problems.

Following the same reasoning, the knowledge which clinically trained men possess concerning normal and disease processes should be applied to the solution of basic problems as well as to those of clinical significance.

The recommended individual approach to experimental problems may not appear possible in view of the limitations of specialized training already discussed. Actually, this may be true, but only during the initial stages of development. One of the chief attributes of an organization of this type is the day-to-day association of scientists and clinicians which eventually leads to mutual understanding of both fields. This, in turn, develops in each worker the ability to think in terms of both the clinical and scientific aspects of a problem. It is only when this point is reached that each member of the group is able individually to pursue effective independent research, and the laboratory as a whole is competent in all major phases of a specialty.

A secondary function of the staff is postgraduate teaching of basic science applied to a medical specialty. The laboratory staff should have the same teaching relation to the clinical specialty as the staff of the preclinical department has to medicine as a whole. For example, physiology might be limited to physiology of the eye or the urinogenital system, as the case may be. Experience in different branches of the specialty pre-eminently fits the laboratory staff for this task. It may also be desirable

for the staff to assist in postgraduate teaching in clinical subjects, but all teaching should be so arranged that it does not occupy over approximately a quarter of the staff's time; in any case, it should not be permitted to bring research to a standstill.

The number on the staff will vary with the physical facilities of the department and with the financial support, but three is probably a minimum number for an effective unit, and four or five is better.

A laboratory staff in neurology, for example, might include two clinicians having different research interests, a physiologist, an anatomist, and a biophysicist. Arrangement should be made so that other members of the clinical department and investigators who might be assigned from cooperating preclinical departments could also participate. Temporary associates supported by term grants could assist the research group. Adequate technical assistants, secretarial aid, and an animal room attendant should also be provided.

If the laboratory unit is to function effectively, and if mistakes which in the past have resulted frequently in scanty and mediocre research are to be avoided, special consideration must be given to academic standing, remuneration, and tenure of the staff.

The system of rank in most clinical departments differs significantly from that in preclinical departments. It is customary in the former to have a professor, one or more assistant or associate professors, and a much larger number of assistants and instructors. In most instances the latter devote but a small fraction of their time to teaching and little or no time to research; they may continue without advancement in rank for life. Many of the men holding these lower ranks are outstanding physicians in the community, and their reputations are independent of their academic rank in the medical school.

In the preclinical departments, on the other hand, the staff ordinarily is much smaller and consists chiefly of men who devote full time to academic work. The same system of rank prevails, but the assistants, instructors, and usually assistant professors are young men. For them, rank determines their standing in the profession.

Since the staff of a fundamental research laboratory consists of career men, their academic status should be comparable with that of career men in other academic fields rather than with that of their co-workers in clinical medicine. In order to describe more accurately the type of work performed and to avoid the appearance of discrimination, it is preferable that the titles of the laboratory staff be different from those of the clinical staff, e.g. professor of neurological research, on the one hand, and professor of neurology, on the other.

The income of men in research does not approach that of the average practicing physician. If qualified physicians are to be attracted to medical research, a reasonable salary and satisfactory security in tenure is essential, particularly if they are to remain in this vocation. Salaries must compare favorably with those offered in basic science departments and in industrial research laboratories.

In such matters as academic standing, remuneration, and tenure the policy of the research laboratory may well be patterned after that of the preclinical rather than the clinical department. In problems of organization, on the other hand, this is not true because of distinct differences in personnel. For example, the staff of a biochemistry department ordinarily consists solely of biochemists, that of a bacteriology department only of bacteriologists, etc. In contrast, the complexity of fundamental research in the clinical field requires a staff of individuals from various fields. Strict adherence to the vertical system of departmental organization common in academic departments is unsuitable for the small staff of the laboratory. This is not to say that the usual academic advancement through the ranks should be abandoned, but to point out that as each staff member becomes, through experience and accomplishment, an authority in his own right, he should be rewarded with the rank and salary that he might have had if he had remained in his original specialty.

With rising costs, a budget for a laboratory involves some uncertainty. However, approximately $12,500 to $15,000 per year per staff member is probably a good estimate. This amount should cover salaries for the staff, technicians, secretaries, diener, and machinist, and the cost of animals, supplies, and equipment. A laboratory consisting of four staff members would require between $50,000 and $60,000 per year.

It is pertinent now to discuss several less tangible matters of importance in establishing research laboratories in the medical specialties. First, if the basic scientist devotes sufficient time and effort to becoming familiar with both the medical and scientific aspects of a specialty, it is possible that he may not be able to maintain in each the same proficiency as the more specialized individual. It has been said that he is neither fish nor fowl. This criticism might well have been made about the biologist or chemist who first transcended the horizons of his specialty to become a "biochemist," but few would deny that this "hybrid" has contributed more to the development of biochemistry than has the biologist and the chemist. The great contributions to the advancement of knowledge in the scientific aspects of medicine may well come from another "hybrid" who might be called the "medical scientist."

Secondly, in leaving an established field such as clinical medicine or basic science to work in a relatively new, composite field, the staff may experience a degree of professional isolation. If the laboratory is located in a hospital away from preclinical departments, this feeling of isolation is likely to be more acute in the basic science.

It may be reduced by more positive recognition from the clinical staff of the department, by association of the basic science group with members of the preclinical departments, and by the formation of professional organizations created for workers in the special field. Membership in most medical groups is limited to those with a degree in medicine. Since the prime reason for this limitation concerns the practice of medicine, which is not involved, some special status in the local or regional organization covering the specialty should be created for the nonmedical members of the laboratory. This would be mutually advantageous, since it offers opportunities for professional contact and provides means by which clinical members may keep abreast of recent developments in the more fundamental aspects of their specialty.

As interest in fundamental research in the clinical specialties increases, societies for the exchange of papers, and possibly special journals, provide other ways of reducing the isolation. The trend in this direction is illustrated in ophthalmic research by the formation of the Association for Research in Ophthalmology, Inc., and by plans for a special technical section in an ophthalmological journal.

### Scope of the Program

The number of laboratories necessary to bring fundamental research to a state of development comparable with that in other branches of science is dependent upon the number of clinical specialties involved, the proportion of total investigational activity in the fields for which these laboratories might assume responsibility, and the special requirements of any given specialty.

Although departments representing every clinical specialty were not visited, a definite need for increased basic research was expressed in the following fields: dermatology, medicine, neurology, ophthalmology, orthopedics, otolaryngology, pediatrics, and urology. Since several others might be added to this list, a total of 10 specialties is a reasonable estimate.

It is beyond the scope of this paper to discuss the research needs of all of the specialties or to attempt a close estimate of the proportion of the total research in any one of these fields which ultimately might be performed in these laboratories. However, in ophthalmology four such groups might well be organized. If this specialty is reasonably typical of the average, the number of research laboratories in all of the fields would be of the order of 40. On the basis of the budget previously given, this would call for an annual expenditure of approximately $2,500,000.

### Immediate Objectives

The financial requirements of the proposed program may appear to present insurmountable difficulties to any action which could be taken without government support. Furthermore, because of the undeveloped and unorganized state of basic clinical research, it would be premature to attempt to put into operation so comprehensive a program or, indeed, any alternative plan comparable in scope without a preliminary test on a smaller scale. To this end, steps should be taken now to set up one research group in each of four specified clinical fields to serve as nuclei around which expansion could be planned. These four laboratories would cost approximately $250,000 per year and should be planned for a minimum period of 8 years, making a total expenditure of about $2,000,000. They need not be located in the same university, but the existence of a central authority to coordinate the whole effort and maintain unity of purpose is essential. In operating these test laboratories information would be obtained concerning the effectiveness of this method of conducting research which might well transcend in importance the scientific results. However, the latter alone should more than compensate for the effort made.

Provision should be made at specified intervals to evaluate progress in these laboratories. This evaluation and plans for enlarging the program might be made by the sponsor in cooperation with an independent board created for the purpose.

The immediate questions are: What means are available for establishing four initial laboratories, and who would be responsible for such action? It might appear that government support is the logical answer. However, except in those fields of interest which fall within the domain of the War or Navy Departments or the Division of Public Health, few governmental funds are yet available for general distribution to medical laboratories. Since the research interest of the proposed program does not coincide with that of these government agencies, private support must be obtained. This is not without its advantages, as the greater flexibility and altruism permitted by private foundations are especially valuable during the formative period of a new venture.

In general, funds may be sought from three main sources: private individuals, public subscription, and foundations. They may be in the form of outright endowment or periodic contributions.

Appeals to private individuals and the public have proved successful in obtaining funds for studying cancer, poliomyelitis, and tuberculosis. There are two drawbacks to the use of this method for establishing the four test laboratories. First, an appeal to the public requires a highly organized campaign which depends on a previously existing organization; secondly, since most laymen and many nonlaymen do not understand the broad aims of fundamental research, the response is likely to be poorer than it has been when money was solicited for investigation of specific diseases.

There are numerous foundations whose purpose it is to further medical research. The history of medical education and research relates many instances in which the

successful inauguration of a new venture depended upon receiving financial support from a foundation. The proposed program probably is no exception. However, its financial needs pose new questions to the foundations, for large sums are required over an extended period. In the past, most foundations have given only relatively small sums for specific projects and for periods rarely exceeding five years. The prospect of obtaining the requisite funds for establishing fundamental research laboratories in clinical medicine may depend upon the degree in which the foundations will allow precedent to influence their present policy. Whereas this policy may well have been a wise one in the past, an eminent authority, Dr. Alan Gregg, in *The furtherance of medical research* (1941), has advocated that "the larger foundations return to making capital grants for endowment and for both the larger and the smaller foundations to make fewer grants for terms of seven to twelve years instead of one to three." In so far as these viewpoints are accepted by the foundations and point to a trend in their policy, it is to be hoped that aid from them to expand fundamental research in clinical medicine will be forthcoming, at least until the public feels obliged to assume the responsibility for the support of research and thus makes it possible for the scientist to devote himself to science and not to raising funds.

The responsibility for *initiating* significant expansion of basic research in clinical medicine and for formulating a program worthy of support from the foundations or the public rests primarily with those forward-looking clinicians and basic scientists who realize that continued progress in medicine depends upon the discovery of new basic principles.

# Environment and Food Intake in Man

**Robert E. Johnson**[1] **and Robert M. Kark**
*Harvard Fatigue Laboratory, Soldiers Field, Boston*

ALTHOUGH IT HAS BEEN ASSUMED THAT feeding habits among men are modified by differences in climate (*4*), very few quantitative, reliable studies have been reported on the effects of different environments on the voluntary food intake of men doing the same type of work.

Between 1941 and 1946 reliable data have been collected on the average day's food which healthy, physically fit soldiers (ground troops) chose to eat from the rations provided in temperate, mountain, desert, jungle, arctic and subarctic areas in North America, Europe, and Asia. Most of these data were obtained during surveys and Army ration trials conducted intermittently throughout the war. Calculations were made according to the method of Berryman and Chatfield (*1*).

The present communication is taken from a critical review of the nutrition of United States and Canadian soldiers prepared in 1946 for the U. S. Army by Johnson and Kark (*3*). Fig. 1 and Table 1 show some data on the nutrient intake of healthy, physically fit, young North American soldiers who lived and fought in different environments in different parts of the world. Each point in Fig. 1 represents the average caloric intake for groups of from 50 to 200 men who, at the time of examination, were fully acclimatized to the particular environment in which they were living and who showed no signs of nutritional deficiency. For the purposes of this discussion, data have been selected only from groups of men who were receiving an ample ration in wide variety and of such quantity that they could have eaten more if they had wished to do so. This ideal situation in the feeding of troops was, unfortunately, not always achieved. The data show a striking correlation between the average voluntary daily caloric intake and the mean environmental temperature to which the groups of men were exposed. The range was

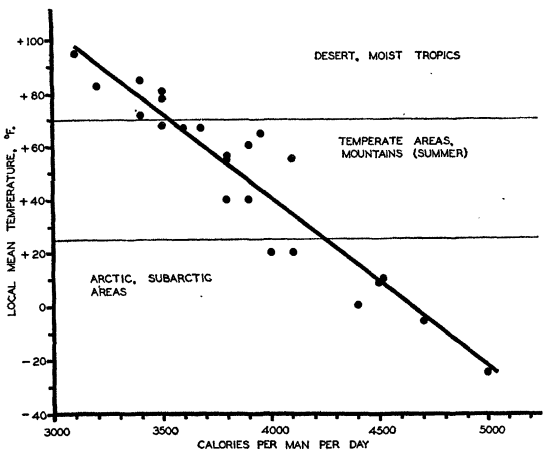


FIG. 1. Voluntary caloric intake, North American troops (averages for groups of 50 or more men).

[1] Present address: U. S. Army Medical Nutrition Laboratory, 1849 West Pershing Road, Chicago, Illinois.

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