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A WHITHER REPORT ON THE RESEARCH DIVISION OF THE CLEVELAND CLINIC: A COMMENTARY ON RESEARCH TODAY

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THIS report reflects the view of one person, currently the Director of Research of the Cleveland Clinic. I hope, however, it is not a minority point of view. It represents my cogitations after 16 years of experience in the Division. Some facets of only contemporary interest are included to provide a truer picture of the problems we face from year to year. Some small rubs and irritations must surely show through. There has been no attempt to cover them up with soothing verbiage. Rather, I have attempted to present an instant in the reality of the conduct of research.

The report is meant for those everywhere who are interested in the organization of research, for those who support research, and for those who suffer from the diseases that will be benefited by the fruits of this sort of research.

The Changing Scene in the World of Research

I have had the interesting experience during my professional life of seeing a complete reversal of public attitude toward research. When I started in 1920, the attitude was one of complete indifference on the part of the public, and most physicians. As you are well aware, since about 1946, our era has suddenly become an "age of science." I am sure I hardly need convince you of this when most "growth" companies are now spending from 6 to 10 per cent of their wealth on research. Former President Eisenhower's Science Advisory Report reflects this change when it says, "Scientists have become one of the nation's most valuable resources." President Kennedy's health message calls for a "vast expansion of medical research." And lastly the Report of the President's Conference on Heart Disease and Cancer makes the firm recommendation for "a much higher level of federal appropriations in support of medical research in the fields of heart disease and cancer and a commensurate increase in voluntary contributions."

And what are the nation and the present administration going to do about it? Again, I quote, "American science in the next generation must, quite literally, double and redouble in size and strength. This means more scientists, better trained, with finer facilities." There can, in my opinion, be no doubt that this doubling has already started. As one report puts it, "The training of scientists takes longer than it used to and the facilities needed are much more complex and expensive." It is only a question of a short time when competent research workers are going to be at a great premium. It is possible that many places will find themselves with fine facilities but nobody of excellence to use them, which is the reverse of the situation just a few years ago.

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Our problem in our own laboratories is to create, and to maintain, an atmosphere in which creative research can be most effectively done. Deflection from this purpose, no matter how seemingly cogent the argument, can only result in less important and less original output; it is the net output of creative work of excellence that determines the worth of a research division.

Investment in Science

Until recently, support of research was considered charity. A sharp change has occurred and it is now a prime investment. In fact, there have been almost no speculations, let alone investments, which have paid off so handsomely both in money and improvement in the material aspects of the social scene. "We are only just at the beginning of the use of scientific investment in the large sense and the returns it can bring in are literally incalculable." It seems to me that we are at the beginning of the scientific revolution, just as a century and a half ago we began the industrial revolution. From the actions of Congress, the Bureau of the Budget, and the President's directives, it is now clear that research support will not be withdrawn according to a caprice of Congress. We, in particular, were unwilling at one time to accept any further support from government because we feared it to be "soft money."

No one today can say how rapidly this great industry of discovery will grow. The President's report says this: "Any shortsighted calculation of return on investment is likely to be self-defeating. Scientific progress does not occur in any neatly predictable way." The evidence is now clear that support from government on a large scale is occurring and will accelerate.

There are also changes in the way money is being given and how it may be used. The trend is to give maximum flexibility and stay away from the restrictive plans of a few years ago.

Basic Versus Applied Research

Until quite recently, and to a degree even today, an argument was being carried on which purports to prove that so-called basic or "program" research stands in direct opposition to applied "practical" or "clinical" research. This has been a futile waste of time and has misled many well-meaning people. The quicker the whole question is dropped the better. One striking characteristic of our new scientific age has been the gradual disappearance of this distinction. There is no such thing as "impractical knowledge." The same individual is often both a "pure scientist" and, for example, an engineer. He may well be both an "impractical" pharmacologist and a good bedside doctor. Thus, distinctions of this sort are poor ones on which to build plans. Gains in knowledge must not be labeled and pigeon-holed as practical or impractical. Rather they should be kept before all, for use as needs arise.

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REPORT ON RESEARCH

History of the Organization of the Research Division of the Cleveland Clinic

Doctor Corcoran and I came to the Cleveland Clinic early in 1945 to organize an entirely new research division. Those were war years and we had to "make do" with what we had, not with what we would have liked. Thus, many changes that should have been made were not made. We have remained in a number of respects on the original "make-do" war footing.

We had what we think a unique plan. Instead of breaking the Division up into a series of small, unrelated cells called "departments," the whole group was thrown together as a unit, working on a central theme. The group was organized around the problems, in our case hypertension, arteriosclerosis, and brain chemistry. This scheme, over short periods, is sometimes not so flattering to the ego of the individual as is strict departmentalization, but in the long run has proved more satisfying because of greater work output and sense of achievement resulting from the actions of the whole group. I am convinced that the effectiveness of some professional investigators under this system is much greater, in terms of advancing the problem, than that of several other types of organizations. This is not a plan for the "lone wolf" type of investigator.

To keep our work oriented toward the problems of medicine, beds in the hospital were set aside for our patients and we started our own outpatient group. These patients are fully cared for by us and have been the starting point of all of our major research problems. This arrangement has proved of inestimable value. In this way the Division has achieved a certain homogeneity in which the disciplines that represent it all contribute to the same general operation. Patient care and structural organic chemistry rub elbows, as do physiological and physical chemical research. I believe this a unique and valuable contribution to the organizational scheme of medical research and, in the future, the principle should not be lost. Pulling away of the individual from this structure is easy to do for the sake of immediate expediency, and if this is carelessly acceded to, the whole structure shortly disintegrates. I feel strongly that if this unifying principle of organization around the solution of major problems is lost, the research effort in our case will be greatly reduced in effectiveness. I can assure you from long experience that disintegrative forces are constantly at work to break the group effort into small independent units.

The Nature of the Problem

Small organizations are always faced with the problem of how much of a major problem they should undertake to solve. Because of the fact that the understanding of cardiovascular diseases had not advanced signally until the past decade, we felt impelled to take a broad approach, hoping that the problems would narrow and would deepen with the passing of time. For example, diet soon became a

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major aspect of the problem of heart attacks. To study diet in its relationship to patients, a research kitchen had to be set up. Because of the success of this work, the Government asked us to plan, and to set up, a major dietary study aimed at broad testing of the proposition that practical change in the American diet might lead to lessening of the numbers of heart attacks. You will now see why there is no dividing line between basic and applied research.

Let us take another problem, this time concerned with hypertension. We had for many years been studying the problem of the control of the caliber, or diameter, of blood vessels by the nervous system, for if the caliber is reduced, blood pressure goes up, as during a fit of rage; and goes down when the caliber increases. We were constantly on the lookout for chemicals that would block this action of the nervous system. Many hundreds were tested in association with drug manufacturers with greater, or lesser, success. At present, one drug, called "guanethidine," has proved in our patients as well as in our dogs with hypertension, to be highly effective. As more knowledge is gained through research, still more useful drugs will become available. We now feel confident that with proper care, most high blood pressure can be controlled and the patients' lives greatly lengthened.

I want to impress on you the variety of skills that is required to solve problems as varied as these. It is for this reason that we have enlisted the aid of organic and physical chemists, biophysicists, pharmacologists, pathologists, physiologists and statisticians—all concerned with the same problems. There is need for still more of these disciplines to be added, which is what I have called "the conduct of research in depth."

We have tried, inasmuch as is possible, to take problems from our patients and transfer them to the laboratory for solution. It is for this reason that our clinical work has been such an important aspect of our research. But when the problems reach the laboratory, we must demand that the research be worthy of the subject. By this, I mean research of depth and penetration. Until recently, in the field generally, there has been much superficial work that will not withstand deeply probing criticism.

The Problem of Maintaining a Research Staff

We face a serious disadvantage in research in clinic practice, when compared with universities, in that we do not have the continuous stream of stimulating young minds to work with us. Most of our staff is recruited from young people who have recently acquired their degrees. Sometimes we choose well and the man becomes a permanent part of our staff. Often we must let them go because we do not believe they will grow into the caliber of men we want on the staff. Thus, we look at all new people as candidates for staff, in marked contradistinction to universities; which, because of numbers, must let many go elsewhere.

Twenty years ago the research market was glutted with brains. Today it is

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just the reverse. I suggest that during the next 10 to 20 years, the major problem in research is going to be to find, and to hold, high-grade talent. In the past few years we have lost some valuable people. However, this does not mean that we have come to the end of opportunity in medical research. The quality of the young men and women to pick from has not seriously deteriorated, despite the fact that other research laboratories and, in particular, the universities now have the money with which to compete.

My strongest plea is to insure that young people constantly pass through the Research Division so that a few can be selected and kept. If this is not done, the quality and quantity of the staff could deteriorate dangerously. It is all too easy to pass from excellence to mediocrity without even realizing it.

How Big

I have said for the past 16 years that there is a limit to the size of our Research Division. I have never believed that the most creative research came from enormous, impersonal institutions, universities or otherwise. There are certain simple criteria that I look for: the organization should be small enough so that:

1) Everyone can know everyone and see most nearly every day.
2) Few formal meetings are necessary.
3) Mutual exchange of information can occur expeditiously and informally.
4) Equipment may be used by everyone with minimal effort and rules.
5) The spirit of unity is everywhere to be found.
6) Elaborate and impersonal rules and regulations do not have to govern the group.

In my opinion, the physical boundaries of the Division are about right. Improvement here and there is very desirable, and in some cases essential, but these are not big things. Flexibility is essential. Research, as you well know, does not lend itself well to rigid planning. When you find you can plan too easily, the signal flags of danger are up; you are no longer doing creative research. If you are going to get in a rut and follow it, choose the rut well because you will probably be in it for a long time.

No one can say what a research division will be like in 10 years. I would hope no one would want to say. I am certain if there are sensible, competent people running it, the Division will add importantly to knowledge of its chosen fields. If you try to substitute rigid plans or committees for able people, I will predict the Research Division will cost the same, or more, but its productivity will have deteriorated seriously. A negative and constantly restrictive atmosphere created by a nebulous fear that somehow research will overgrow other activities of a great clinic is groundless, and if credence is given this fear, it can ultimately erode the creativity of groups such as ours. This is an aspect of research that is

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hard to sense and to recognize. Perhaps it is best characterized by the "spirit of the place." Lose it and you will soon find how important it was.

Except in its broadest sense, I cannot tell how big a research division should be. I can tell you how good it should be. I would prefer to leave to my successor the planning of his future because I cannot tell whether he will be concerned with "outer space medicine" or the more earth-bound problems which have so excited us. I would prefer to count on the common sense and wisdom of personal leadership than attempt an impersonal blueprint for the future.

I would want no curb on the intellectual bigness of a research group but physical bigness has definable upper limits which should be determined by common sense in the maintaining of excellence.

Consolidation of the Research Division

I believe that all organizations that are effective must have flexibility. I have already said that I do not believe a research group should grow beyond certain definite limits. We must not, however, confuse growth with change. Drop-out of effective personnel is inevitable, and younger people must always be in training so that replacements may be made. Equipment must be kept up to date. There must always be some room for modest expansion for the workers who prove themselves most effective. Without this the good ones will certainly be lost.

Communication with the Scientific and Lay World

One of the chief functions of science is to communicate with other scientists the world over. To do this requires the most painstaking care in the preparation of reports on the work that has been accomplished. In our profession, a man's reputation among his peers is one of his most cherished possessions. Not to understand this is to miss much of what goes on in the world of science.

"Personal glory" is a much misunderstood and abused phrase. I can only give you a word of advice; among good scientists, avoid the phrase, as you are almost sure to misuse it and to create misunderstanding. The creation of an "atmosphere of respect" is a difficult and often subtle thing, much less easy to measure than so many dollars' worth of a product or service. Laymen often tend to sneer at what seems to them a personal and selfish characteristic of scientists. If, on the other hand, you will think it through, I suspect you will reach a deeper understanding of the nature of science and scientists.

Perhaps I can best illustrate the nature of the problem that all good investigators face by our own experience in the synthesis of angiotensin. About 20 years ago we discovered this important substance along with Braun-Menéndez in Argentina. In the ensuing years, work has continued steadily but very slowly in our laboratory. At times only one man was concerned in the isolation of a substance that may well be the cause of a major type of high blood pressure. Our

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total group of investigators was that small. Such a situation would be inconceivable in the field of, say, cancer research. About eight years ago a well-equipped and intelligent team of workers at the Crile Veterans Hospital also started on the quest. We were for a long time unaware of the competition. Concurrently a team in London, England, began as well. The result was that within a short period the structure of this complex substance had been determined by these groups. The only way we could save our position in the field was to synthesize angiotensin. With only two people to carry this out, we were amazingly fortunate to be able to accomplish it at the same time a group of nine chemists at the Ciba Company in Basel, Switzerland, announced its synthesis. Had we not been lucky and the two men not highly skillful, we could well have lost out entirely in the field which we opened. While the outsider may say what difference does it make who discovers something, remember the research worker has only one salable product and that is his reputation.

The desire to communicate, of course, in part springs from the fact that until people accept a piece of work it is not included in the body of verifiable knowledge. To do it well is to create an atmosphere of respect. Writing and lecturing are two of the few legitimate ways of exhibiting the excellence of research to doctors and laymen. There is often a tendency to disparage this type of public relations because tangible results are often hard to measure. One of the simplest measures is the kind of young men and women who want to join the staff of the Cleveland Clinic. Good ones are attracted by the contributions and persons of excellence on the staff. Good doctors want to belong to a distinguished group.

There is still another aspect of communication which concerns the participation of the research staff in the large scientific societies, government commissions or councils, or organizational activities such as the "American Diet Study." I believe these activities are of great importance but should be so regulated that they never become more than a side line. When, in general, they cannot be done in the "evenings or week-ends," except under unusual circumstances, they should be cut back.

Project Research

I have described the program of research carried out by the Division itself. There is need for another device to implement the research needs of physicians in the Clinic. This is done by a committee composed of members from both the Clinic and the Research Division.

The proposed project is submitted to the committee in writing. After careful and sympathetic study, it is either accepted or returned for revision. An adequate budget is available to finance these projects.

Since this system was inaugurated some five years ago, there has been marked improvement in the quality of the projects submitted. Relatively few are

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now denied, and most of them are completed. Years ago the mortality among research projects was shockingly high, chiefly because the would-be investigator had more momentary enthusiasm than scientific training. Our clinical staff has now learned that research has much drudgery connected with it and that to do it successfully it must for the most part be done with the physicians' own hands and brains. Research *in absentia* is seldom a success.

Financial Support of Research

I shall observe simply that over a period of 15 years the Research Division out-of-pocket expense to the Clinic has been unusually steady. We hope that research endowment will grow. A few gifts have, from time to time, been received quite unsolicited. This has been a deeply heartening experience. The rest of the money has come from government, and at first, there was great apprehension about it. To repeat, at one time, we actually turned our backs on it. I think we all realize now, that this is "hard" money. Despite this, I hope that private donations will continue to be an important and even a vital part of our budget. The loss of private giving would, in my view, be a disaster.

I want to make my position on a budget crystal clear. I agree that a budget should be employed. I do not agree that a "top level of spending" for the next 5 or 10 years can, at present, be set.

I hope that the Research Division will keep one goal in mind — to run the Division as effectively as possible within the limits of its physical size and the mental capacity of its staff. Money is only one of the aids to the furtherance of these goals, and to set it as *the* limiting factor is irrational.

I want also to call attention to another form of fiscal problem. From time to time we have been asked by government to administer, or to participate in, some cooperative major research problem in the national interest. Recently, for example, we were requested to set up a national diet experiment. A specified sum was given us to pay committee meeting expenses and the expenses of an executive director. Little of our time is needed for this activity but a certain amount of bookkeeping is required which is adequately paid for by overhead allowance. Under no conditions, however, do I think this sort of monies should be considered as part of the research budget. To do this would destroy the whole philosophy of the spending of money on research.

The point I am trying to emphasize is that without the use of good judgment and common sense, a budget can be made to have a leaden effect, and become an almost constant source of irritation. I believe that judgment concerning expenditures must be based on long scientific experience, and that within the limits of the money available for research, the Director and the Advisory Committee must make major decisions in collaboration with the Administrative Office.

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The Purposes and Goals of a Research Division

1. Medical and surgical care is as good as the research which supports the body of knowledge on which it lives. The "better care of the patient" is therefore one of the primary purposes of a research division.

2. Research itself is worth doing for its own sake, if for no other reason than that it enriches the human spirit.

3. Research provides a constant stimulus to better and more penetrating medical practice. Its educational value is great.

I would also call your attention to the President's Commission on National Goals, the so-called "Wristen Report." Not a single working scientist was on this Commission, yet they observe that:

1. "We should allot a greater proportion of our total effort to basic research —. We should recognize that our creative activities in science and all other fields will be more productive and meaningful if undertaken, not merely to be ahead of some other nation, but to be worthy of ourselves."

2. "Available scientists must be used more efficiently. The practice of wasting highly trained people in jobs below their capacity, particularly in some defined related industries, must be eliminated."

3. The Commission feels that the next decade will see new scientific breakthroughs which may change our lives, our industries, our jobs and perhaps our whole thinking.

4. "In an age when few political decisions can be made wisely without some scientific grounding, no college graduate should be totally ignorant of science."

This report, like several others, gives a clue as to how some people of insight and integrity are thinking.

Recommendations

1. Help to create an atmosphere in which research of the greatest excellence can be conducted.

2. Insure that there is a constant supply of young people from whom staff will ultimately be recruited. A plan for postdoctorate training would be most desirable and probably will be essential.

3. The unity and constancy of purpose of a research division should be carefully guarded. There is always danger that the activities will become splintered and the advantages of working for the common goals of solving particular problems be lost.

4. Growth should be limited to small, flexible increases or decreases in staff and equipment, wherever the need seems to exist; perhaps this had best be called "consolidation."

5. The budget principle should be kept. The spending of the budget should be under the control of the Research Director with his advisory committee in

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consultation with Clinic administration.

6. The activities of a research division should not be too closely integrated with the income of the parent clinic. It should be recognized that enough funds can be obtained from outside sources to insure top efficiency.

7. I strongly recommend that every effort be made to infuse an atmosphere of stability so that every few months there is not another period of re-evaluation of research and "soul-searching" by one or another groups. The work load of research is purposely set at such a high level that even small distractions are wasteful.

8. I close this report with the thought that I do not expect that all problems will be solved with one large resolve. I hope that many of the principles on which an excellent Research Division should operate can ultimately be agreed upon and be codified, but certainly not all. Further, I hope we never get away from the philosophy in which I so firmly believe: that you cannot substitute rules for individual human decisions, and that committees cannot run an organization. To me, a research division will be only as good as the individuals who do the research and who participate in its management.

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