

THE ROCKEFELLER UNIVERSITY

SOME COMMENTS AND PROPOSALS

This discussion was not planned initially to be of the nature it now turns out to be. The plan was to examine some general trends in The University programs and suggest some extensions which seemed important for further development. The more medical programs were to receive particular attention and this portion of the original plan is adhered to.

Incidental to the preparation of the comment, an opportunity was afforded for conversations with a number of individuals of the intellectual community; some students and some junior and some senior members of the faculty. The support programs were also surveyed but not in detail; and several accounts of The University and its programs were consulted.

The thrust of the general information obtained led to the belief that it might be more reasonable to discuss problems of The University and its further development in a historical and philosophical context than a coldly analytical point of view. The presentation, which results is more useful in that it may provoke discussion rather than propose a simple course of action.

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# I

## Background

The transition of The Rockefeller Institute for Medical Research into a specialized university emphasizing the life sciences appears to have reached the end of an initial phase of organic growth. Changes which have occurred include an increase in the number of research groups, a broadening of the biological and behavioral base of the enterprise, the inclusion of related programs in the chemical, physical and mathematical sciences, and the introduction of predoctorate education. This growth has been accompanied by a lessened emphasis on the more medical portions of the program. The addition of small programs in cultural subjects appears to have been accomplished without particularly influencing the hard science nature of the environment.

At this point, concern for the future of The University is commonly expressed by some of the senior staff and the institution's "alumni," but this unease is not widespread. That which is evident seems to be stimulated by a concern of students and faculty alike for the need to reexamine the roles of The University in a modern society. This is more of a national than a local phenomenon. As best one can judge from limited discussions, there does not appear to be a hardening of any series of simple propositions which might serve as a guide, or, a limit, to further development.

There is general acceptance of the views that the freedom of the independent scientist and general scientific excellence must be maintained; and that the University is "unfinished" and should plan for continued growth.

There are differing views on how growth can best be managed. Some would continue the operations of The University in the dominant mode of the present; i.e. support of the individual scientific units without particular

substantive regard to the activity of other units within the environment. Others appear to be reaching for institutional mechanisms that, continuing the freedom of opportunity for the individual scientist, would favor programs of an integrative nature conducive to greater interaction among a number of the individual groups. There seems to be no particular resistance to the concept that this might foster some coalescence of some activities around broad conceptual statements of program purposes. All favor a flexible approach to development, managed in a fashion that does not violate the internal scientific forces of the field. If a resulting program has quite obvious societal import, then this would be judged to be acceptable to most scientists and desirable to many.

There is also an expressed desire to improve the opportunity for research in the more complex biological systems such as can only be examined in the total animal. Such a desire is particularly apparent in some of the medical groups, the activities of which are generally oriented toward the elucidation of disease phenomena. Others would couple biological studies of the CNS with rapidly evolving opportunities in the behavioral sciences, and the broad extension of these to the primate including man. Without being specific as to substantive program content, a number of scientists favor significant involvement of The University community with problems such as "population" and the "environment." A recurring theme that emerges from many discussions is the role that the systematic exploration of the various aspects of human development might play as an integrative force for many of the present discrete activities.

A general characteristic of faculty views on these matters seems to be a desire to pursue any programmatic change by an expansion of the science base of the institution rather than through a major redirection of personnel and

and resources already available. Some would also seek an increase in opportunity through affiliation with other institutions.

But one general impression comes through quite clearly, there is a mild ferment now in process with no firm lines having been drawn on either a conceptual or substantive level. It seems likely that a restatement of broad University policy covering the substantive content of the University's planning would be appropriate at this time. If the staff were assured that the policies arrived at were to be the result of serious discussions with both the Board of Trustees and the senior faculty, then much staff uncertainty would be resolved in a satisfactory manner. There seems to be no thought that this will not be done.

Extraneous factors contributing to uncertainty comprise the general phenomena of social unrest, and its reflection in the general university community. A triad of internal circumstances also have direct impact on the community. These are:

- Fiscal uncertainty as the result of constraints on federal spending and the inroads of a continuing inflation.
- The intent of the administration to undertake a program of further development but with a lack of understanding, by the senior staff, of the general but substantive considerations which will underpin the plan for development.
- The change in University "leadership," the substantive impact of which is yet to be fully felt.

#### Concerning University Purpose

A general statement of University objectives is feasible. This should be philosophical in nature but probably not prepared as a freestanding document. It would be more effective if the statement were background for the exposition of the proposed extensions of institutional program. The audience



for such a document should be students, staff, and potential sponsors as well as the general public.

Perhaps the most important area to be examined in such a statement relates to the broad purposes of the University and the development of a central view on how its programs and operating philosophy relate to contemporary society and some of the latter's more obvious needs. The need for such a reasoned proposition or series of propositions is not unique to The Rockefeller University. Rather, it is likely that the inability of many a university to state clearly its perception of its own role in society is basic to much of the student-faculty-administration conflict that has evolved. In the absence of a self-definition of purpose and plan, there is much to find fault with in any complex institution and little for the non-dissident to adhere to firmly. The problem of Rockefeller may be particular and pressing despite its small size because it is not a conventional university.

The Rockefeller University may thus be doubly vulnerable. It is vulnerable to the influence of the non-thoughtful dissident that is simply a reflection of its position as a member of the university community. It is also prone to criticism by a few because of its massive commitment to science, and by others because of the fashion in which it carries out this specialized mission. Actually, a sense of broad mission is only dimly perceived by some. Many scientists find the University an effective locus for their own activities but seem to lack a sense of "institution" and a set of "institutional objectives" they can adhere to firmly. Then too, there may be a lack of vigorous support of the University from those who are increasingly disenchanted with the benevolent nature of the power and force of science as these are expressed in the University programs; and also from those without a clear perception of the relevance of research, particularly fundamental research, to the

satisfaction of the overt needs of a contemporary society. These attitudes are not unique to The Rockefeller environment.

Personal security is commonly disavowed by the young scientist as a satisfying end for which to strive and the lack of other clear and worthwhile guides to career development lead to individual doubts and frustrations. These are clearly evident. It is important to note that some of these concerns are really quite conventional, some are derived from a heightened personal sense of social purpose which, in the individual, may or may not be fundamental. The general scientific environment must have a reinforcing influence on this disease. There is a lessening of individual career opportunity in a contracting scientific universe, this in turn is reflected in the extension of the period of dependency of the student and young faculty member. The net worth of limited scientific goals and the relevance of these to a real and brutal more general universe, pose both intellectual and emotional problems to the developing scientist. In such a set of circumstances, short term individual accomplishments may seem to be poor substitutes for a deeper conviction of the importance of, and at the same time a clear perception of progress toward generally agreed upon important goals.

The general university environment tends to foster doubt and inquiry, this is good; has been in the past and will be in the future. But an essential that must be satisfied, for high institutional morale is a complete and profound commitment of the young scientist to the purposes of his environment.

In the case of the general university, this has obvious social utility without becoming committed to social programs in a direct operational mode. This is derived from its general educational programs, its more limited programs of professional and graduate education, its innovative productivity in the arts and sciences and its general acceptance as a center for intel-

lectual inquiry.

The general educational programs are concerned with public education, the provision of teachers for the educational systems of the Nation, and the basic educational experience for a number of essential professions. It may also be deemed to be socially acceptable to many because of the cultural function it serves in the community although, depending on how this function is performed, it can be perceived as an institution dedicated to the perpetuation of an establishment not now found to be wholly acceptable to many. It can be argued that many universities and indeed, the university world in general, does not perform these tasks too well. This is a healthy and quite reasonable attitude. But it is important to note, in terms of the social purposes of a general university, even the most disenchanted agree that the general tasks themselves are essential.

Graduate (and professional) education in the general university provides for the definitive development of scientists, technologists and an array of competently trained professionals in socially essential fields. These activities have a common characteristic, at least in theory. Each of the students touched by an advanced educational experience is expected in proportion to the length and depth of the experience, to be increasingly capable of independent action within his field of choice. Again, there may be disagreement on the emphasis given graduate and professional education by field but little disagreement on the importance of this aspect of the educational process.

The third general university function is more controversial, i.e. research, particularly in the sciences. This is evident when the research is viewed with respect to its utility to society, when the benign purpose of the ultimate product is suspect, or when its purpose is not understood. It can

also be controversial, regardless of its content, when the research is pursued on a massive scale.

Distrust of science is not uncommon in our society. This can stem from simple ignorance or from attitudes leading to humanistic life styles. It may also stem from the view that much research does not have a socially desirable objective or indeed may be anti-social in its purpose; or from the belief that much research does not have clear relevance to the great problems of today. In these views, research should receive a lower priority in the allocation of the limited resources available. Simplistically stated, while some research is good and essential, much is trivial, and some is actually evil. In the view of others, the too vigorous pursuit of research objectives can detract from the competence of the educational process, and the deferral by the university of science tasks deemed to be important and within its competence. Comments such as these are not to be taken lightly by the university world for they are not limited in their utterance to a disaffected few.

The entire array of criticism is not infrequently the main substance of remarks of a few in our Congress and in the state houses across the Nation. In the specific case of biomedical research, criticism is too frequently the common currency of exchange of some deans of our medical schools and some leaders of the medical profession. The biomedical research program is not infrequently viewed by these as a deterrent to the needful expansion of medical education and only a minor contributor to its excellence. In addition, it is charged with the sequestration of an inordinate amount of physician talent thus directly contributing to the physician shortage in the health service delivery systems. Such views may be held to stem from ignorance and to be unfair. Nonetheless, the views are current and do influence the attitudes of students and the general public alike. To date, they have

received far too little attention by the leadership in our universities. The simple though valid statement that "Universities are for learning" (McGeorge Bundy, *Daedulus*, vol. 99, p.555, 1970) carries little conviction when put to the concrete test.

The broad social purposes of The Rockefeller University have not been clearly stated. It must be accepted that the University makes little contribution to general education or to professional education except indirectly in its contribution to the education of faculty for other universities and their professional schools. Further, the student body is limited in size and substantive content. The size of the graduate student body, though substantial, constitutes only about 20 percent of the intellectual community and is heavily concentrated in the biological, behavioral and biomedical fields.<sup>1</sup> Given such a situation, the net worth of the University is largely determined by the productivity of its research staff - and probably more, than less, on this alone.

The research activities in turn, will be increasingly appraised, less from the standpoint of the simple excellence of the units of work - general excellence being expected on the basis of past performance, and more from the substantive content of the research. It is inevitable that such an appraisal will include considerations external to fields of science. These will be required for a general but clear understanding of the relevance of its programs to the great societal problems of our times. In a real way, The

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For purposes of this comment, the postdoctoral fellows can be considered to be a transient portion of the investigative staff of The University.

Rockefeller University will likely be judged by criteria which are increasingly applied to an assessment of the net worth of the nation's total commitment to the biomedical sciences. But the nature of the nation's commitment in this area is undergoing change. Having established a broad program of undifferentiated science in the past two decades, the nation's biomedical scientists are increasingly being posed questions as to the reasonableness of the distribution of their effort within more or less fixed resources: this in relation to the unsolved biological and behavioral problems of medicine; and the applicability of the newly acquired knowledge to the solution of the social and economic burdens imposed by ignorance. A healthy reappraisal of the distribution of our national effort is inevitable as are the program shifts which can be anticipated. Hopefully these changes will be the result of mature consideration of scientific opportunity and not simple expressions of social need. Importantly, in this assessment, it is certain that note will be taken of the maturing behavioral and social fields and the interaction of these with the more conventional fields of biomedical activity as these have developed during the past two decades.

Modest amounts of research in institutions with broad educational programs are likely to be found acceptable without special regard to substantive content. They will be assessed for their direct contribution to the excellence of a lively educational process. But the larger research programs, such as are conventional in research institutes and research divisions, will be subject to a more penetrating appraisal. In applying these attitudes to a consideration of the further development of The Rockefeller University, some questions become quite specific. These relate to whether or not the deployment of its resources is such as to foster a meaningful approach to a selected number of broad problems in the fields of its concern; and whether the problems

themselves are presented in a meaningful fashion. Again, the simple excellence of a series of discrete activities may not in itself be considered adequate.

These views do not reflect the simple view that the University should restructure its ongoing activities in a fashion which would replace fundamental research with general objectives, by applied research with specific objectives. Quite the contrary, this would be both traumatic and unproductive. But, it may well be that such views are important in considering the further development of the University. They may also be determinative of the ease with which it is possible to continue the financing of the present programs and at the same time to provide for an extension of University activity into the future. One way or another, they will have a profound influence upon the acceptance of the University by its sponsors, as well as by some of its staff students.

The major problems facing the University leadership during the coming half decade will be to sustain the excellence of the individual units; and to select a limited number of broad program areas with acceptable general objectives. Each of the latter must be selected with care, giving positive consideration not only to the discrete scientific opportunity, but also to the utility of the broad program in providing an integrative force for some of the existing programs.

It is possible that new institutional programs deemed to be desirable will be of a nature that they cannot be developed wholly within the laboratories and clinics of the University. Some no doubt can but others will only be possible with suitable cooperative arrangements. But then, cooperative arrangements may be desirable in themselves in the broadening influence they can have on The University.

## II

## Early Developments

The University continues, as in the past, to be generally characterized by the excellence of its scientific activities and the distinction of its scientific staff. But, its role, within the broad sweep of science,<sup>1</sup> has changed during the span of its development. These changes include its functional setting within the general Rockefeller interests, its institutional purposes, and its ability to influence the contemporary science of the nation. It is useful to review some of these occurrences, less for the details of historical development than to provide some sense of history as a solid base to view the prospects for institutional change.

The University had its beginning at the turn of the century (1901) as a series of laboratories in chemical, biological and medical sciences aimed generally at the provision of a science base for medicine. The then Rockefeller Institute was one of the nation's four or five science oriented institutions with a capability to modify American medicine. A view of contributions to this is possible only if its activity is viewed as part of a broader, loosely integrated set of activities supported by the Rockefeller interests.<sup>2</sup>

The major elements of these programs, were The Rockefeller Institute for Medical Research, its loosely dependent Hospital and The Rockefeller Foundation with its subsequently developed International Health Division. The programs supported contained a mix of domestic and overseas activities which coupled

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<sup>1</sup>Science is used as a broad term having the dimensions of the sum of research and education within a broad intellectual context.

<sup>2</sup>The General Educational Board will not be discussed.



biomedical research, medical education and public health. The substance of the work performed and supported was related to what were perceived to be the great medical problems of the period.

Domestically, the Rockefeller Institute and Foundation were most productive in the development of new leadership in the coupled functions of research and education as the U.S. medical schools underwent a progressive change from a trade school type of institution to one generally characterized by a high degree of professionalism. These changes followed acceptance of the general concepts of medical education propounded by Flexner. His report, published at about the time of the 10th anniversary of The Rockefeller Institute, emphasized the need for a sound science base in the education of the physician. The Rockefeller interests were important in part because their individual programs expressed a similar point of view and each had well-established mechanisms with which to exercise a determinative role on the medical schools in the process of change. The full influence of these organizations was particularly evident in the 1920's.

The modern biomedical scientist is prone to overlook the ferment in medicine in the U.S. at the turn of the century. This reflected the development of broad areas of relevant science in the laboratories of Western Europe and the continuing scientific deficiencies in most American institutions. But, a beginning of change or at the least, the opportunity for needful change, was perceived by a number of thoughtful professionals at that time.

Bacteriology was providing an increased understanding of the nature of infectious diseases. Organic chemistry had developed a base for the study of metabolic phenomena. Physiology was in the process of defining the interactions of components within complex organ systems and systems control. Pathology had made a good start in the description of the morphological expression

of disease processes and provided a more rational base for the classification of disease phenomena.

The practical utility of this new information in both the development of sound education and in the management of disease was clearly apparent. As a result, there were established a few modern laboratories in each of several U.S. universities and in some of the departments of the federal establishment, i.e. The Medical Department of the Army and the U.S. Public Health Service. Further, the general social value of research was sharply defined for the American public by several occurrences. Yellow Fever, in epidemic proportions, was suppressed in Cuba; a trans Isthmus canal in Panama was shown to be feasible providing prudent disease control was exercised; and the scandals in the drug field and their correction in the creation of the Food and Drug Administration emphasize the general need for science and technology in the manufacture and approval for distribution of therapeutic agents. Meanwhile, the Public Health Service was demonstrating the utility and effectiveness of a quarantine function conducted with proper laboratory support.

These achievements, occurring at about the time the new Rockefeller enterprises were evolving, must have had a profound influence on the character of the initial undertakings. The early objectives, as best one can interpret the intellectual thrust behind the programs, were evenly divided between the development of new knowledge and its application in the resolution of medical or public health problems. Given the flux in education, it is not surprising that they also included purposeful efforts to modify the form and substance of medical and public health education in this country and abroad. The research supported encompassed both the fundamental and the applied but eminence was given to professionals of high competence to determine the courses of studies

that they deemed to be most likely to achieve the desired end result. This juxtaposition of general goals and freedom in the methods of pursuit of fundamental and applied research continues to characterize much of the overall Rockefeller enterprises.

There can be no doubt that these concepts together with a full appreciation of the power of science led to the establishment of the laboratories of the International Health Division of The Foundation in close association with the Laboratories and Hospital of The Rockefeller Institute. This was likely less a matter of convenience than to provide an increasingly important public health enterprise with a broad science base, within an environment committed to the use of science in the resolution of important medical problems.

The period up to the beginning of World War II was extraordinary in the productivity of the Institute programs. A cataloguing of achievements is less important than a sampling which can provide some sense of their major thrust.

Prominence was quickly achieved in areas of organic chemistry, (of natural products), anatomy (cytology), cellular physiology (particularly in relation to membrane phenomena), and physical chemistry (the formulation of theory covering redox potentials). But the prestige of The Institute was importantly derived from equally fundamental research which in addition had quite specific application to disease.

The more medically oriented studies were wide ranging and quickly achieved eminence in a number of fields. These included the study of cancer and the relation of viruses to uninhibited cellular growth; the examination of viral and bacterial disease including the fundamental nature of these agents, the diseases they produce and how these latter could be prevented or modified; the exploration of cardiovascular disease and the related problems of hypertension and chronic renal disease: the general conceptions which

underlie the theoretical, and practical consideration of antibiotics in the control of infectious disease.

Other productive areas of research provided precise methods for the study of biological and biochemical phenomena in health and disease. These were particularly important as a quantitative base for clinical science which, beginning in the teens, developed rapidly in the U.S. during the twenties and thirties. Related to this general type of activity was the penetrating observations leading to the concept of fixed blood groups with its immediate and profound influence on medical practice.

There were other important contributions but those mentioned are sufficient to make an important point. The peculiar genius of the early Institute and its related Hospital was the development of broad programs of fundamental biomedical research within a framework of disease objectives; and to utilize the research activities as a training base for the development of science based medical educators. Broad accomplishments by small groups of brilliant scientists was somewhat easier during the early period than is true today and great leaps were possible with substantially less resources. But this does not detract from the extraordinary accomplishments of the early Institute scientists.

Meanwhile, the Rockefeller Foundation performed an essential role in the developing institutions of medical education and supported selected areas of research both at home and abroad. It is difficult to reconstruct the details of the interacting relations among the several Rockefeller programs in summary form, but it is quite clear that the impact of the entrance of gifted scientists into U.S. medicine from the Institute and Foundation programs was profound. The programs of the International Health Division of the Foundation and its loosely related Peking Union Medical School and

University had an equal influence on U.S. and overseas science particularly in South America and in China, India and South East Asia.

These Foundation programs were critical in providing an international base for the medical sciences and were particularly effective in providing effective linkage between scientists and research activiteis in the U.S. and Western Europe.

They also had a profound influence on public health practice in many then called underdeveloped countries; public health practice based on an elucidation of the mechanics of disease and its transmission. The Foundation's overseas programs gave particular emphasis to malaria and other parasitic diseases and to viral disease, (more particularly yellow fever).

With this general background one can examine the happenings since World War II which produced such striking changes in the Rockefeller enterprises during the past quarter of a century. The Foundation activities will be discussed first so as to provide continuity in a consideration of University programs in the later sections.

The Rockefeller Foundation - Post World War II. There were a number of outstanding U.S. medical schools in the late 1940's. Also, the federal establishment was rapidly developing significant science support programs both at home and abroad. These factors diminished the impact that could be generated from within the private sector on medically oriented institutions in the United States. At the same time there was obvious need for temporary aid to institutions of Western Europe and long term needs for support of health activities in an increasing number of "developing" nations.

In such a situation it is not surprising that the Foundation reduced its support for medicine in the Continental U.S. rather sharply and extended its aid in both South America and Western Europe. There was also a critical

shift in program content as it became increasingly clear that poor nutrition was an important and world wide problem. But a continuing interest of the Foundation in medical education is apparent in the development of a model program for the production of physicians and related medical personnel in Cali, Columbia, and the later development of a new type of Medical institution in Tanganyika which seemed suited to the needs of Africa. During this period, the development of medical school staff was aided by selective research and fellowship support to a number of medical schools in South America and in the newly evolving nations in Africa, the Far East and Southeast Asia.

The evolution of these overseas activities as the primary programs of the Foundation led to the abolishment of the International Health Division and then the closure of the latter's laboratories at the Institute. This was accompanied by a curtailment of the direct research of the Foundation and a relative expansion of grant supported activities.

But, as the last quarter of a century evolved, support of activities in Western Europe and South America (except for Cali) was progressively withdrawn and there was a change in program emphasis. The Foundation continued a general interest in medical education, but increasingly emphasized agricultural technology and the relation of this to the satisfaction of nutritional deficiencies. No doubt the programs in Mexico which resulted in hardy, highly productive hybrid strains of corn had a profound influence on this later development. The Mexican experience was strikingly successful not only in its impact on the immediate problems of malnutrition but also on the broader fields of agricultural reform and food technology. These accomplishments, in addition, had an important influence on the economy of the country.

The more recent programs in the food production area seem likely to be equally successful. certainly in South East Asia, the Philipines and India. These advances are centered about laboratory support for the development of

hybrid cereal grains in the Ford-Rockefeller supported International Rice Institute in Manila, agricultural and nutritionally oriented laboratories in India and Thailand and backup support from a limited number of U.S. laboratories. Immediate application of the technological advances in agriculture coupled with the development of indigenous sources of fertilizer and more sensible water use have already resulted in a striking increase in food production particularly notable in these areas. The advances now seem to be well along toward integration, by locally developed scientists and technologists, into conventional agricultural practice.

The results of this shift in program emphasis by the Foundation now seem secure. They are presented in summary form to emphasize the wisdom of coupling fundamental research (in this case plant genetics) to a broad activity which seeks to solve a difficult and important practical problem. The programs also demonstrate that the concurrent development of local scientists and technologists can secure long term continuing progress with indigenous support in foreign countries as well as in the U.S. In the light of these successes in South East Asia and the Far East, and the development of productive agricultural programs in Africa and the Near East it would be surprising if the programs of the Foundation were not the subject of a further change in emphasis.

Serious concern for the quantitative and qualitative aspects of a nation's food supply must be matched by comparable concern for population size and population growth and the impact of these on technological development. In this view, it is not surprising that the establishment (in 1952) of The Population Council<sup>1</sup> was followed by the development of a set of scientific

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<sup>1</sup>This council is a separately funded activity the primary support being derived from the Rockefeller Foundation in association with the Ford Foundation.

activities within a context of the social problem. As the Rockefeller involvement in this problem has increased, it has been a factor in modifying the attitudes of both official and private agencies particularly in the U.S. Substantial federal resources are now available and the problem is given high priority by the Ford Foundation.

Comparable concern for the population problem has only recently become apparent in a few U.S. universities. The possible involvement of The Rockefeller University with such a program will be noted below at greater length. At this point it is emphasized that little is to be gained for the University by its entrance into the field unless a program can be evolved which is congenial to already existing activities, and if the program is given high priority in the core of the University's objectives. Present University involvement is minimal. The University serves as a host to some of the scientists of the Population Council but the program, as now conducted, is largely one of operational convenience.



## III

## Current Prospects

The Rockefeller University, Post World War II. It is clear that, as with the Foundation, the role of the Institute in American science changed with the re-establishment of the nation's programs in the biomedical sciences after the disruption of World War II partly because its resources became increasingly less distinctive.

The hard core of university science in the United States, initiated during the thirties, was expanded rapidly with federal support in the post war period. This was evident in the availability of more extensive resources, the increases in pre and post doctoral education, and the increased size of university faculties. The expansion of research opportunity was common to both "private" and state universities, their associated professional schools and to a number of evolving research institutes. Extensive changes in the substance of the science enterprise paralleled the increase in research opportunity, first in the physical and then in the biomedical sciences. The full flowering of the federal influence was particularly notable in the 1955-1965 decade as biomedical research moved from the part time avocation of a few to a full professional occupation of many.

It is pertinent to review briefly the effect of these changes on the volume and substance of research during the total period (1945-1965). This period is critical in that it spans the post war decay in the influence of the Institute, the enquiry into its future (1952), the decisions which led to a change of institutional program (1953), and the early years of University development.

The immediate post war period (1945-1953) was profoundly influenced by the increasing availability of antimicrobial agents and appreciation of the increasing social and economic burden of chronic illness. These influences resulted in a shift in research emphasis to the chronic diseases. The biological complexity of these diseases, the general disenchantment of University scientists with the target research of World War II, and the increasing availability of new methods for the precise quantification of biological phenomena, were determinative influences in the evolution of a fundamental biological approach to these problems.<sup>1</sup> As the result of an expanded industrial effort a large number of therapeutic agents which were developed empirically during the fifties and early sixties which, though not preventing or curing important acute and chronic illness, permitted the amelioration of the acute episodic manifestations of both types of disease. Also, large surgery with its attending drama became commonplace. During this period too, the nature of many diseases were more clearly defined and an array of viral vaccines were developed. Some of the latter were striking improvements on those previously available (rabies, influence, yellow fever), others (polio, rubella, measles, mumps) were wholly new.

These practical advances relieved the pressure for "results" and freed the biomedical scientists to use the internal dynamics of science as a major guide in the evolution of their research programs. These time related phenomena are not commonly understood by many scientists.

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<sup>1</sup>The importance of so-called "basic research" was highlighted by the evolution of the National Science Foundation and the prominence given "basic science" by a number of Federal mission oriented agencies.

As the post war research programs approached maturity, other changes in medicine were taking place, (particularly during the 1960-1965 period), and those were to have an important impact on the support of biomedical sciences. There was an increasing appreciation of the need for a modification in the methods for the delivery of health services from systems which provide for the management of episodic illness to systems that had as their objectives the maintenance of health. This progressive shift in objectives in the service area is reflected in the type of continuing care provided in many specialty clinics and which can find definitive expression in the full scale provision of health maintenance by newly evolving health care systems. But such systems run counter to the dominant concern of most physicians for a continuation of a fee for service system and have not as yet been fully exploited.

Nonetheless and important for present purposes, is the fact that the changes in the health care delivery system which are in prospect make increasingly possible the long term study of the emergence of chronic disease and its natural history. These new systems will facilitate studies on the modification and amelioration of chronic illness through the long term use of therapeutic (and dietetic) regimens. Other studies of a quite fundamental nature will also be feasible.

These are beneficial effects, at least in prospect, but there are others with strikingly adverse influences. The progressive involvement of federal agencies in providing an economic base for an increasingly high cost function is an important factor in limiting the support of its biomedical research enterprises. These occurrences have several consequences. Less "real dollars" are now available to support the increasing research opportunities and an increasing demand for short term results have become increasingly apparent. At

the same time, medical institutions are faced with the dual responsibility of expanding physician production and remedying defects in the service systems. It is not unlikely that those problems will be prominent in the future determination of federal support for the coupled functions of research, education, and research.

During the period of rapid program development (i.e. 1955-1965), there also occurred a profound shift in the clinical investigation of disease. Initially largely limited to clinical observation, increasingly emphasis has shifted to the active manipulation of the concerned biological systems under highly controlled conditions. Such a shift in clinical research content is nowhere more clear than in the increasing use of "normal volunteers" in parallel with the patient with disease in the study of the operation of well defined biochemical and physiological systems at rest and under quantitatively imposed stress. Such studies provide precise information which can be utilized in the subsequent modification of the biological systems in useful fashions to prevent or modify serious disease. Out of these general trends, and over the longer period under consideration (1945-1965) many clinicians have been transformed into a clinical scientist with a full capability of operating at all three levels of fundamental, applied and developmental research. Importantly too, the well trained clinical scientist can now approach the problems of disease with a broad understanding of the relevant fundamental sciences and a full capability for intimate interaction with his more biologically based colleague.

During this same period striking changes were taking place in the more biological portions of the biomedical sciences. The entrance of scientists with mathematical, physical and chemical skills into these fields provided both the views and instruments of precise science. Biochemistry with its

concern for overall phenomena of cell metabolism, simple enzymes and the kinetics of enzyme reactions in limited systems has been extended to encompass the quantitative exploration of biochemical and biophysical phenomena on a molecular and cell organelle level.

The newly emerging field of molecular biology, drew upon, and in turn influenced in a revolutionary fashion the disciplines of microbiology, immunology and genetics. These, in turn, provide new insights into the molecular basis of some diseases and the opportunity to explore others in a more definitive fashion.

Perhaps even more revolutionary have been the changes in the behavioral sciences and their potential influence on biologically oriented counterpart areas of science. This is nowhere clearer than in experimental psychology. The era of the "brass psychologist" is long since past. Present experimental emphasis is on such broad areas as the development of the cognitive faculties, perception, learning and language and on the behavioral base for a variety of social phenomena. Direct application of some of these advances to problems of human development are quite evident. Such studies provide the base of others with a view that the plasticity of the central nervous system for a substantial post natal period is a common ground for exploration both biologically and behaviorally oriented scientists. Viewing the opportunities objectively, one can only wonder if the delay in coupling of these fields may not be largely due to our unrealistic compartmentalization of science.<sup>1</sup>

Importantly, an aggregation of biological and behavioral scientific effort could provide a new and rational base for the restructuring of our conceptions of the proper rearing of the child and of the fundamentals of our

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<sup>1</sup>As early as 1962, a broad interdisciplinary discussion group was established through NIH support within the framework of the American Academy of Arts and Science. This continues to be a highly productive activity.

general educational processes. The information for these changes is much more likely to be provided by biologically oriented behavioral scientists than by the more conventional students of education. Equally important, the results of such a hard scientific exploration of these abstruse processes can be expected to yield definitive results that are directly applicable to the definition of, and rescuing operations possible, for the retarded child. Most certainly they can provide a more precise definition of the role of environment (including nutritional as well as behavioral factors) in the development of the retarded, the usual, as well as the superior child. These are truly exciting prospects.

A large number of other areas of science are equally characterized by broad opportunity in the fundamental sciences, some with direct applicability to the human in distress. Included in these are:

- The further development of our understanding of viruses and their interaction with cell information systems as a basis for the understanding of their role in carcinogenesis, and their likely contribution to some of the devastating diseases of the central nervous system;
- The further exploration of the intermediary metabolism of food stuffs and the directive factors leading to the associated and interactive problems of obesity, atherosclerosis and diabetes;
- The provision of a rational biological base for the understanding and further development of an array of therapeutic agents which influence a variety of systems including those that affect mood and influence frank disturbances of behavior resulting from systematic psychiatric disease.

but these are only a sampling.

The lessons to be learned from many of the recent advances are applicable to the planning of future research necessary for the solution of serious problems. For any major problem it will be necessary to provide a precise understanding of the operation of one or more quite fundamental biological systems,

to extend this to encompass a clarification of the directive influences which modify the operations of the system within the intact animal and to define the role of specific biological systems in the generation of disease.

Quite apart from such developments and their influence on the substance of contemporary science, science in the process has acquired a new dimension. This is derived from a clear capability, given time, to solve the many important problems of disease. This is more so than a decade ago and the relevance of science to the many medical problems of today is more easily perceived. Unfortunately, this also serves to stimulate a public whose appetite has been whetted, but not satisfied by the advances of science.

The general character of the scientific environments out of which further major advance will likely emerge are equally clear. The biological, and the behavioral and medical skills required must have a broad base in the physical sciences, mathematics, computational skills and engineering. But, studies of this complexity will require large laboratory resources, and access to many animal models supplemented by well organized human populations. Such an array of talent and resources can emerge from the invisible colleges of science which themselves provide for loosely arranged collaboration. They can be developed through federal action in well formalized programs of collaborative research. Or, at times they occur within an individual institution because of a general concurrence of scientific interest and an institutional policy which fosters the belief that in the allocation of resources, some can be utilized to foster a limited number of programs with broad purposes.

When the advances in the life sciences, particularly those related to the nature of man and his problems, are viewed in this manner it is not surprising that the newly developed University Medical Centers have been and hopefully will continue to be particularly well suited to take advantage

of these opportunities. Such institutions may be faulted for their over concern for science and their less than adequate performance in the educational and service areas. But, it is to be devoutly hoped that in remedying these latter deficiencies, they will not destroy an otherwise superb organization for the biomedical sciences of the future. They are particularly well suited to support the evolution of broad programs of fundamental research and at the same time foster the interaction of scientists operating at the extremes of fundamental and quite practical endeavor. These new science organizations have no need to adhere to any particular organizational pattern. They have a capability to evolve without concern for the scientific character of their professional staff, or the substance of their research undertakings. They need not adhere to any particular predetermined size or number of scientific groups that may be required for the prosecution of a given set of problems. Then too, dealing as they must with the application of the leading edge of science to the practical problems of medical care and the education of physicians their social purposes are both secure and evident.

And yet they operate at a serious disadvantage. This is derived from the fact that they are not primarily research institutions and increasingly they must respond to a need for a greater abundance of physicians and to needed modification of the health care systems of the nation. Then too, their role in the production of medical specialists frequently tends toward undue fractionation of programs.

But to return to the evolution of the Rockefeller Institute -

Some of these phenomena which relate to the evolution of science in the 1955 to 1965 decade, were becoming evident in the early fifties. The deficiencies in the organization and programs of the Institute were clear even in the face of the continuing productivity of the Institute staff. But,



the progressive effects of these influences on the character and quality of the Institute programs were evident in the operational limitations on the ability of the Institute staff scientists to participate in the rapidly progressive revolution in American science which was beginning to take place. Of particular note was the fairly rigid functional structure of the Institute, and a limitation on the size of research groups and the resources that could be made available. Conventions concerning the source of support imposed strict limitations on the ability of Institute scientists to participate with their university colleagues in the broad increasing support provided from federal sources.

It was within such a frame of reference (1952-1953) that a searching enquiry was made into the operations and future prospects of the Institute and the continuing need for the replacement of its senior leadership group. This set of inquiries led to several general decisions. These involved a modification of the basic bylaws of the institution, permitted the initiation of formal graduate education, looked to external sources for funds to expand the physical plant, the support of an increasingly large group of scientists, the ultimate creation of The Rockefeller University and influenced the program content of the new University.

The program of the Institute expanded rapidly thereafter, the University's primary purpose being, to emphasize the broad reaches of the rapidly developing biomedical sciences and at the same time to provide a broader science and cultural base for the expanding environment.

New opportunities were developed in fields of chemistry, physics and mathematics and biology on a reasonable scale. History and logic were introduced on a more limited scale. The biomedical fields were substantially broadened by these changes and the activities of many groups enhanced by an

increase in group size and the provision of new resources. This expansion of activity was particularly evident in the biological area with emphasis being given to the many aspects of science emerging in the fields generally grouped within "molecular biology." Other expansion encompassed studies on the development and operations of the central nervous system. Also, a good beginning was made in programs within the behavioral sciences. But the more medical aspects of the University's program did not flourish in a comparable fashion although continued support was provided in the infectious disease area, in studies concerned with lipid metabolism and atherosclerosis, in liver disease, and in problems associated with drug dependence.

The bulk of the new activities and the expansion of already existing activities followed the conventional pattern of the earlier Institute in that each group was established within a fairly well defined area in science. As with the "older" activities, collaboration of groups was encouraged but general "goals" that might encompass major joint enterprises of several groups were eschewed. In all these changes, excellence in scientific effort was sought for and achieved. In many ways the program evolution was quite similar to comparable developments taking place concurrently in many first class general universities.

One cannot quarrel with the purposes set forth by the review committee in its report to the Board of Trustees (1953). This reflected the rugged individual views and life styles of many if not most of the leaders in the biological sciences at that time. A pertinent passage in this report is as follows:

"The Institute should be continued, developed and strengthened, with its research emphasis at the long-range fundamental level in areas of medical research which its independence, resources in men and material, and lack of departmentalization make it uniquely qualified to explore, with the double function of pro-

ducing trained investigators as well as research publications. To the extent that resources permit, it should support additional selected activities outside the central establishment which will further contribute to the accomplishment of its objectives.

"The present policy of freedom from all programmatic, or project research should be continued. Each individual scientist should be free to shift the direction of his research in accordance with his own best judgment."

Nonetheless, some would comment along somewhat different lines today.

Research can be pursued as an essential part of a lively program of general and graduate education and this must be done in the general University which requires a sound science base for the primary educational purpose of the institution. However, when research is supported and performed on a massive scale, the requirements for an adequate program have additional obligations. These relate to the general purposes of the research and its broad relevance to societal needs. To decide otherwise is to conclude that science, supported directly or indirectly by society is a thing apart from society and cannot thrive in close association with the latter's problems.

It is particularly true that the development of any broad area of the biomedical science, even when it has "its research emphasis at the long-range fundamental level in areas of medical research," must have some general purpose in mind. It is also clear that such a purpose for its accomplishment to be complete, most generally will involve a mix of activities; some pursued on quite a fundamental level and some on a more applied level; and depending on the area of study there may be a component on a developmental level. Further, such a general purpose will rarely find healthy expression within a scientific environment except in the case of small discrete groups of scientists in the absence of one or more integrative forces. These can be generated so as to have a substantive influence on the direction of the many components that necessarily will be involved in the solution of any broad

problem but need not stifle individual initiative. Finally, it is quite clear that many of the diverse problems of medicine can provide a variety of integrative forces for such general purposes. The acceptance of one or more of such general purposes has the dual advantages of providing both a scientific guide to the evolution of the program and a social value to the overall enterprises.

It is to be emphasized, that such science organization as is necessary to provide for the achievement of one or more general purposes of a complex nature, can heighten the scientific excitement of an environment rather than depress it. But this requires sensitive "management."

Such a view does not envisage the compression of all of an institution's activities into a series of stereotyped scientific organizational forms. Rather, the view expresses the conviction that many areas of the biomedical and behavioral sciences can only find full and definitive expression if the science organization is such that several discrete science objectives can be encompassed within a broader general purpose. Such a general purpose must inherently have great importance, and must be able to encompass the narrower scientific objectives of individual groups involved. When such a task is well performed, it does indeed make the whole greater and more satisfying than the sum of its component parts. Bluntly stated, the achievement of such a goal in any area of science requires enlightened scientific leadership and not direction in the ordinary sense of the word.

Contrary to these convictions, the application of the philosophical design for the developing University (p.29) and the rapid advances and changing nature of biomedical problems and biomedical capability have both resulted in a progressive movement away from the fundamental character of the programs that characterized the Rockefeller Institute before World War II, and which

continue to characterize the activities of the Rockefeller Foundation today. Both of the latter adhered to general purposes as a set of concerns in the allocation of resources and in program development. The positive moves of the University as it sought to provide for "research emphasis at the long range fundamental level in areas of medical research" wrought changes of considerable importance. The broad base was indeed acquired but the expansion of the base was accompanied by a progressive withdrawal of the University from medical problems of broad significance, and the lack of development of other integrative forces which might be useful in the provision of effective interaction of discrete groups of scientists.

In consequence of this, major contact and continued involvement with the great problems of medicine by The University's scientists have become attenuated. The successful prosecution of such problems requires broad resources which are neither provided the medical groups in being nor the environment of the University. The long term survival of effective "medical" activities in such a set of circumstances, is highly dubious, thus throwing into sharp relief a set of problems that must be solved by the University, its executive group and its senior faculty. Furthermore, the changes in the University programs coupled with the program changes of the Foundation, i.e. their more or less total commitment to the international field and the closing of the I.H.D. laboratories at the University, have interacted to provide a radical change in basic operating relationships of these two Rockefeller organizations.

Contrary to the continued prominence of social relevance in program formulation by the Foundation, the major thrust of the Institute's extension to a University has been toward scientific excellence of discrete research units in lively areas of biological and behavioral science as ends in themselves.

The elements of program that have emerged tend to increase the penetration of our understanding of many areas within these sciences but some obvious connections with many pressing problems of the real world have not been developed.

It is important to note and indeed to emphasize that the addition of graduate education to the programs of the new University does not appear to have been determinative of the source of evolution of the institution. Rather, the determinative circumstances relate to the changes of research content of the institution and the broad development of biomedical research in other settings as the biomedical sciences have come of age during the past two decades. It is not unlikely though that graduate education suffers, as does the research itself, from overfractionation of the fields of endeavor.

These views on the development of the University's programs in the past and their present opportunities can be briefly summarized in a simple series of statements and a simple series of propositions.

1. Against a rich background of achievement in the biomedical sciences and medicine, the Rockefeller Institute has evolved along lines that are a simple extension into practice of the recommendations of the advisory group in 1953.

2. Rapid growth has since taken place. This has involved a broad expansion of staff, the provision of more adequate resources and the formal introduction of pre-doctorate education; all of this was accomplished within the concept of a specialized university emphasizing the broad reaches of science with general relevance to medicine, broadly defined.

3. As a result of this development, the present University is composed of talented professionals with multiple discrete scientific objectives in the physical, biological, behavioral and medical sciences.

4. The thrust of science in general during the past decade has resulted in the definition of many problem areas in both biology and medicine, the social importance of which is only matched by their complexity. This in turn has created opportunities which are beyond the capability of small to moderate sized individual research groups, and poses questions as to the reasonableness of extending into the future some of the operating conventions of the past. An alternative, is to determine whether there are broad purposes which, if accepted by a number of new and old groups, might serve as healthy integrative forces for a portion of the University's program.

5. A search for such program purposes should be undertaken with several objectives and several principles in mind. Relative to objectives:

- These should be considered within a scientific context that gives particular emphasis to ongoing activities.
- But other opportunities should also be examined looking less to short term (0-5 year) developments than to middle range (5-10 year) and long range possibilities.
- These considerations should be modulated by an independent appraisal of the relevance of the programs considered to societal need.
- Advantages should be taken, in any redirection of a portion of the University's program, of the opportunity this may provide in reacquiring real and continuing contact with the programs of the Rockefeller Foundation.

Relative to the principles:

- Research of excellence such as is conceived requires scientific leadership of a high order and broad commitment of a number of cooperating units of work to some common purposes. This cannot be directed in the ordinary sense of the word nor be effectively imposed upon a scientific environment.
- Further, the development of research programs around several general purposes should not be undertaken with the view of encompassing all or indeed the majority of scientists within the present intellectual community. Much of the present activities of the University should be supported for itself and because of the significance of the activity on the national scene.

6. Concluding this section one can say that the University faces the general decisions noted above and the very specific decision which follows. The increasing complexity of the more medical sciences is quite obvious. Applying such considerations to the present medical activities of the University one can only conclude that the resources now available to these groups are generally non-competitive with their counterpart in the University. Nor are the resources adequate to satisfy the medical portions of most of the large programs that would appear particularly suited to the environment. If it is not possible to expand the scope of these more medically related activities and improve the resources available to groups involved, they should be closed out as the result of definitive executive action. They should not be permitted to decay through processes of attrition. Some of the medical areas do not now possess the critical mass of scientists or the resources necessary for the continuation of an effective program even with limited objectives. Alternatively a salvage operation might consider the remedy of some of the major deficiencies through collaborative arrangements with other institutions. But, while this might solve the immediate resource problem, it should not be considered to be a permanent solution to the problem.



## IV

## Great Problems

The truly great problems of today do not derive from science. Some follow success, such as population growth incidental to control of disease and temporarily at least, a more adequate food supply; or, the uncontrolled use of science based technologies and a consequent despoilment of the environment. Still others derive from the affluence of some nations which accompanies technological excellence, and the lack of an ability of other nations to achieve an acceptable level of self-sufficiency.

Only portions of these problems can be stated in terms of the opportunities for scientific advance. Contained within the life sciences is the opportunity for fundamental changes in our comprehension of biological and behavioral phenomena such as may result from the development of clarifying generalizations useful in unifying what now are quite diverse areas of effort. The central role of cell information systems in our understanding of many problems is certainly one of these of recent origin. The infectious origin of much disease is another; this evolving in the final quarter of the last century.

When viewed in this light, it is possible to list some important areas of ignorance in the life sciences. Some samples with particular biomedical parameters can be stated in terms of disease;

Mental health and mental retardation,  
Cardiovascular diseases,  
Cancer and,  
Debilitating diseases of the Central Nervous System.

In terms of biological or behavioral phenomena;

Human development,  
Environmental degradation and,  
Population growth and its consequences.

Or, in terms of the inadequate operation of particularly relevant systems;

Medical education and the  
Delivery of health services.

Several features are apparent in such a partial listing. The items are simply translatable into a set of very broad purposes which can be utilized in the development of research programs. With such broad purposes, the derived programs will be comparable broad and obviously complex and only suited for analysis in terms of national needs and their satisfaction. They are less useful as a guide to the specific development of institutions. Nonetheless, a broad comprehension of national needs and the roles science may play in their satisfaction must be well understood by scientists generally if science is not to be considered a thing apart from society, and lacking in relevance to societal need. Relevance when used in this context is not a "tired" and meaningless term. Rather, when properly used, it can be a conceptual strength in providing a rational base for a broad effort and in the design of institutional programs contained within the larger national effort.

For, though a set of national needs may have little consequence to the day to day activities of the individual scientist, and the satisfactions he derives, they can have meaning to institutions within which science is pursued on a massive scale. In this view, the institutional setting for science, can be characterized by randomness or by serious purpose; and the personality of the institution will be largely determined by the extent to which either of these views is dominant. Generally speaking, though the excellence of an individual scientific activity may bear no relation to the presence or absence

of explicit institutional purposes, the latter may be important in determining the sense of institution within the intellectual community.

Despite these caveats on utility; the simple listing of major problems with medical dimensions is useful. Particularly when expanded to encompass more specific items within a general problem. An examination of these can provide some interconnections of narrow areas of endeavor which are useful in the consideration of broader programs which may be suitable for a single institutional setting. As examples of opportunity, cardiovascular disease and human development will be briefly discussed. Then brief consideration will be given to some non-categorical areas of science.

Cardiovascular Diseases - Atherosclerosis. Problems posed by the cardiovascular diseases can be accommodated within a consideration of a small number of specific disease conditions; atherosclerosis, hypertension and a C-V disability due to infection. These diseases are the direct cause of approximately 1.0 million deaths a year, atherosclerosis alone accounting for about half the total, and are said to produce disability in about 30 million people in the United States.

But there is little purity in such an analysis. For example, disability due to atherosclerosis is commonly attended by the concurrent problems of the retina, the heart and the kidney. Further, diabetes, a metabolic disease, is prominent in the causation of atherosclerosis and together these two make substantial contributions to the overall toll of disability and death. To complicate the matter further, there is no doubt that obesity contributes to the incidence of atherosclerosis and hypertension as well as to that of diabetes.

Nonetheless, out of this complex of related diseases, certain unifying concepts have emerged in the past twenty years which provide a solid base for systematic exploration. There can be no doubt that the atherosclerotic process has as a basic biological underpinning, disturbances in metabolism with spin offs in the interconversion of food stuffs on the one hand and departure from the normal in the transport of lipid on the other. It is equally evident that this complex of diseases are modifiable by diet, drugs and hormones. Undoubtedly the "disease" atherosclerosis represents a "final common path" which has its origin in diverse biological phenomena. Included in these diverse biological phenomena there seems to be certain biological susceptibilities which are transferred from parent to child by poorly understood genetic information systems. The most striking examples of this are to be found in familial lipid diseases and in diabetes.

There is no doubt that the systems involved in these diseases are quite complex but not such as can be expected to defy their ultimate elucidation. Indeed, the very complexity of the systems underlying these disease manifestations, their coupling with other biological phenomena that result from specific disturbances in metabolism provide an array of biological models amenable to searching biological and chemical manipulation.

The ultimate solution of the problems of atherosclerosis may well be the development of information which permits their rational management by a combination of reasonable diet and the specific addition of accessory food factors comparable in general conception to vitamins. But these latter substances, not being essential for normal development, would be directed toward the modification of either metabolic or lipid transport mechanisms or both.

A characteristic of contemporary research in this area is the general lack of comprehensive programs that can provide a realistic approach to an obviously complex biological problem. This is understandable but makes little sense when the broad opportunity is considered.<sup>1</sup>

Human Development, similarly, is a problem which is inclusive of many and diverse activities. Nonetheless, it can provide a philosophical center around which a variety of problems undertaken within individual institutions can be given broad meaning.

One such set of related activities might be grouped around the phenomena associated with the initial phases of human development. In this case, concern might be evidenced for fertility, fertility control and the associated phenomena of implantation and early pregnancy. Programs of this general type would necessarily find expression in the study of the physiological circumstances of conception and early development as well as the examination of agents and devices which are candidates for the limitation of offspring. Logically these latter studies would include the systematic study of the acceptability, the effectiveness and the hazards of procedures utilized less as a statistical exercise than in terms of the biological and physiological systems involved. Such an approach would not envisage the establishment of the massive studies. These are not suited for a single institution and though they have both practical and scientific interest are more suitably conducted within a national frame of reference.

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It may be of practical importance to note that the National Heart and Lung Institute has recently formed a committee to enquire into the problem with a view to the development of a ten year program. This committee, which first met on July 9, 1970 will be operational for about one year. A certain consequence of this action will be a diversion of funds, even in the face of a general shortage, to the support of well conceived programs in the area.

The later stages of development are equally exciting. Although our ignorance of these happenings are greater than our knowledge, it is quite clear that mammalian development is a continuum which encompasses both the fetal and early childhood periods. This latter type of development has increasingly occupied the interest of the biologist and behavioral scientists alike. However, joint undertakings by these two groups of scientists are few.

Biologists, in their increasing concern with the sequential phenomena attendant on development, have grouped their activities about a number of discrete nodes. Some of these are concerned with:

- The development of immunological competence, both humoral and cellular, and the separate and combined relation of these to the susceptibility of the developing mammal to infectious disease.
- The development of primary and secondary sex characteristics, the interaction of these to the details of the development of the CNS in utero and the plasticity of postnatal growth as this is influenced by early manipulation of the endocrinological environment of the developing mammal.
- The postnatal development of the CNS, an obviously unfinished organ at birth, and the effect of environmental influences on both the architecture and functional capabilities of the brain and the reflection of these in behavioral phenomena.
- The development of new animal model systems which permit earlier access to the developing mammal for a wide variety of biological purposes. During the past several years, working colonies of marsupials (usually the opossum) have been developed and are just being introduced into biological studies as a standardized biological form.

The behavioral scientists have recently found the processes of early development even more intriguing in studies which include a variety of model systems, (birds, rodents, primates, humans). It is clear that the behavioral characteristics of the adult and indeed his intellectual capacity is largely influenced by events happening in the early days, months and years of life.

But again, the phenomena examined to date serve more to define the importance of this period of development and its suitability for a wide array of behavioral studies than to clarify the underlying mechanisms involved. Land marks in this area are important though few in number. The most striking involve the phenomenon of "behavioral imprinting," the sequential determination of sex characteristics, and the demonstration of the early and definitive influence of early social experience on intellectual development.

These general aspects of human development (i.e. the study of the early period) are available for profitable exploration by both biologists and behavioral sciences particularly as joint enterprises. The opportunities in these areas are great and the information to be derived so important to concepts of child development and the structuring of the child's early educational experiences that much more serious consideration must be given to the field. This type of emphasis most generally requires the declaration of institutional purposes since the resources required for definitive programs are both extensive and costly. (See also Section III).<sup>1</sup>

There are other areas of equal importance that are particularly notable in the circumstances surrounding human development, two of which relate to nutrition; one the genesis of chronic obesity, another the association of poor early nutrition and a limitation on intellectual development. Both of these have high scientific content and at the same time the information derived from studies will have very practical consequences.

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<sup>1</sup>Such a broad series of studies having as their ultimate purpose a more rational understanding of the educational process would be of direct concern to the Office of Education, the newly developing National Institutes of Education, and the Ford Foundation.

In a very general way, it can be shown that poorly nurtured offspring develop to small size at maturity and, at least in the case of the human, are thought to suffer intellectual handicaps not remediable at a later age. The obvious impact of such a set of circumstances on the inadequately nurtured minorities in this country and citizens of whole nations abroad is clear and of first order importance; that is, of course if it can be shown to be indubitably true.

But considering human development from a mechanistic point of view, an intriguing problem emerges. It is likely, in the progressive unfolding of the information system in sequential development, certain stages of CNS development are particularly vulnerable to biochemical insult, and quite likely the insult by one or more quite specific nutritional deficiencies. This can take place either in utero or postnatal development. Viewed as a parasite, it may be that the fetus is less susceptible if it can draw upon maternal tissue to satisfy its essential needs even in the presence of moderate maternal deprivation. This is a reasonable hypothesis and at least has the virtue of being amenable to examination in experimental animal model systems and in the human.

During the postnatal period however, when the plastic nervous system can be influenced by a variety of environmental influences, the situation is quite different. The reservoir of essential nutriment is limited to the dietary intake. Again, as a working hypothesis, it seems unlikely that the total caloric intake of the developing child is as important in CNS (and behavioral) development as the availability of quite specific nutrients during quite specific times in the development process. Alternatively, it is quite certain that a severe limitation on total caloric intake will divert otherwise essential nutrients to simple energy producing processes.



Importantly, these possibilities are amenable to fairly precise exploration in well organized biological and behavioral studies of child development.

But, it is possible to expand almost endlessly the major problems attendant on early human development. Actually the term, though commonly used, has so broad a connotation as to be useless except for general conceptual purposes.

One must pause at this point in the general presentation and remark: "But, what has all this to do with fundamental research." Such a remark might stem from those biologists who are quite right in believing that much of the growing edge of the biological sciences is concerned with the study of phenomena at a molecular level. And this is more than a fashionable comment to make. But here too, there are areas of science which can profit by a suitable selection of groups and scientific personnel with the view to utilize a broad problem as a loosely contrived integrative force.

And as an aside and before exploring this point further, it may be said that the exploration of molecular phenomena will be essential for the ultimate understanding of many problems of human genetics, the definitive examination of agents which influence fertility, the elucidation of the sequential phenomena of the determinative forces involved in cell growth and differentiation and in organ development, as well as the details of the determinative forces that provide the biological base for intermediary metabolism and more particularly for lipid transport mechanisms. In these latter instances the techniques of the molecular biologists and his insight into biological processes become portions of a broader program with program purposes directed toward the elucidation of more complex systems.

But, to return to molecular biology as such, one can touch briefly on the operations of the systems concerned with DNA -----> RNA -----> protein replication systems. The operations of these systems are sufficiently intriguing, important and complex to occupy the total intellectual capability of large numbers of scientists. And, there is no doubt that deeper insights into the fundamental characteristics of many important and vital biological systems will emerge.

The studies can be wholly contained within their own physical and chemical context, and the interaction of such scientists is commonly with others working at an even more fundamental level. The latter are concerned with the refinement of spectroscopy, crystallography, microscopy, nuclear magnetic resonance and complex organic synthesis so as to be able to define the physical and chemical characteristics of individual system components. They may do this simply to understand the detailed structure of interesting biologically active compounds or to learn the nature of the structure which permits it to perform some unique operation in the system from which it is derived.

Such information is obviously important and essential if one is to understand the physical arrangements of the components of a system. These will, in turn, influence both the reaction kinetics, and the energetics of the system and the products that can be derived. The opportunities for progress in such endeavors are exciting and most certainly should be pursued.

But provision for other studies in the field can also be made. These might deal with problems at much the same level of biological complexity but would be more concerned with the operation of these primary systems in the related fields of immunology, virology, genetics and the genetic basis of disease and disease susceptibility. Other studies could be undertaken

which relate to the implications of these systems to information processes. concerned with sequential phenomenon determining cell development, the phenomena of growth and its disturbances.

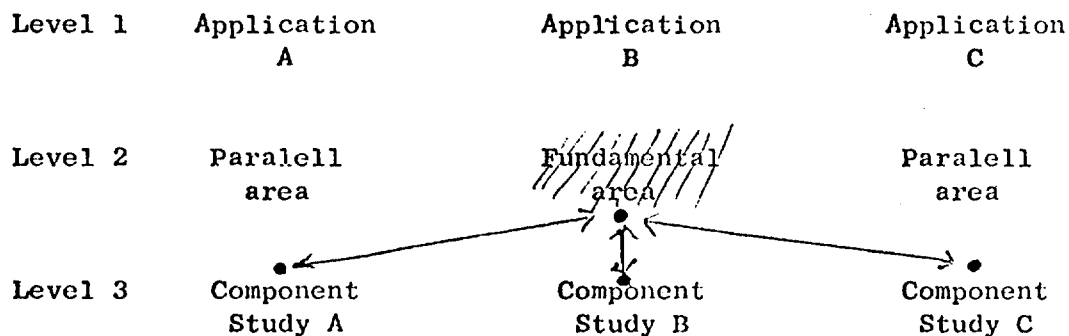
Continuing this thought, and moving from the general and fundamental to more specific studies in the applied area, it is apparent that the results of such studies have application in the clarification of very abstruse problems the solution of which is important for the prevention or management of serious disease. Likely candidates for such studies include the examination of these phenomena in relation to:

- Metabolic disturbances which underlie a variety of molecular diseases generally characterized by mental retardation, by disturbances of lipid metabolism and its association with atherosclerosis, diabetes and a number of other disease entities.
- Immunological disturbances resulting in a number of autoimmune diseases.
- Disturbances of growth, perhaps with a view to understand the process of carcinogenesis.

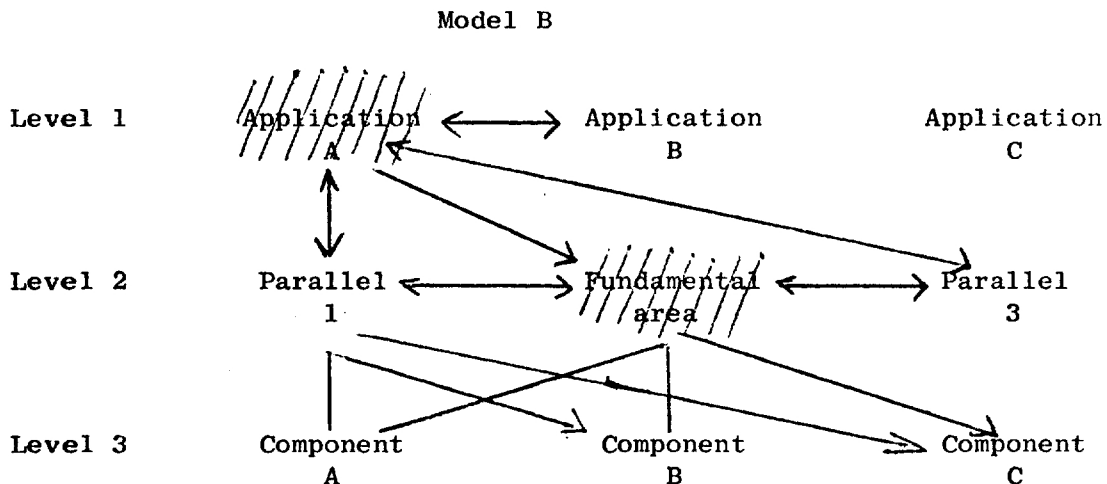
With this brief background, a general point can be made. The normal mechanics of the evolution of new knowledge of a fundamental nature can be of several types.

It may be restrictive, as in Model A :

Model A



Or, it may be more general, reflecting the developments in the restrictive field but also providing for interconnections with other activities that reflect a broad purpose as in Model B:



Model B portrays a typical biomedical research program B pursued at the fundamental level 2, as an element in a more complex interactive series of related studies with logical bridges of activity laterally with adjacent fields, with more fundamental inquiry of the components of the system (level 3) and with the array of activities having interaction with one or more complex systems perhaps associated with human biology in health or in disease. (level 1).

In such a situation the decision that must be made by an institution is quite clear. It may conclude that the associated fields are progressing as rapidly as can be expected through the normal interplay of scientific forces. Alternatively, the institution may conclude that it can, through the judicious selection of purposes and the meaningful allocation of resources provide for substantial increase of the effectiveness of a fundamental field and at the same time, subserve one or more general purpose. The quality of the science may be excellent in either case. However, if the latter decision is made the institution has acquired a general purpose beyond the

Simple exploration of the biologically unknown. Importantly too, it can provide broader resources for a set of related activities which share some common purposes than when each activity is carried on in isolation one from another.

Few scientists doubt the ability to plan a move from a specific observation to a more fundamental level of enquiry in order to explore the general phenomena involved in an initial discovery. However, scientists are too frequently skeptical about the effectiveness of planned development of broadly associated fields. It must be admitted that the latter is a harder end to achieve, and also that attempts in this direction are speculative.

It is nonetheless clear that spectacular insights to quite fundamental problems are not infrequently derived from very complex systems when these are readily available. Recent observations within the DNA -----> RNA --> --> protein system make this quite clear.

The key to this system, the ramifications of which have dominated biological thought during the past quarter of a century, was derived from a qualitative observation on a complex system, i.e. the conversion of one strain of pneumococcus to another which bred true, through the use of a specific nucleic acid.

The unravelling of the structure of DNA, the concept of a system with RNA having a template relationship both to DNA and the derived proteins, the relation of all these to structural elements within the cell, and the complex of specific enzymes essential for the catalysis of these reactions, were all high adventure and required an extraordinary biochemical and biophysical effort. The effort literally involved hundreds of scientists, both in competition and in collaboration with one another. Yet, there were other contributions which

were essential and which were derived from a study of more complex systems. Some of these were concerned with metabolic phenomena of bacteria and their dependent viruses, and the demonstration of the biological characteristics of naked DNA and the modification of DNA viruses in the cancer field with a controlled exchange of protein coats. These were indeed very complicated phenomena to arrange for and to interpret but they gave much point to the studies that were limited to the isolated systems themselves.

Other equally important data of a qualitative nature have been derived from the applied fields. One was the introduction into the cell information system the genome of a virus that itself otherwise disappears. A more recent occurrence is demonstration of the reverse of the DNA -----> RNA process, with the availability of RNA dependent DNA polymerase, and the finding that this is the property of a number of cancer producing RNA viruses.

Demonstrated first for the virus of Rous sarcoma, then for the virus of Rausher mouse leukemia, it is now known to characterize the RNA of at least six RNA tumor viruses. It would appear that the core of each of these contains an RNA-dependent DNA polymerase capable of constructing DNA. This reverse channel of information permits the derived DNA to serve as a pro virus or intermediate in the replication of the RNA virus. This is an extraordinary finding which has broad implications in several reaches of biology, particularly in immunology, quite apart from its impact on problems contained within the cancer field.

There is no doubt that major and striking advances at a fundamental level are attributable more to individual insight (or to serendipity) than to the details of a planned scientific environment. But this need not be taken as the exclusive principle for the design of scientific organizations.

It is equally true that providing resources are broad, and this is important, many fundamental advances can be anticipated to derive from the persistent pursuit of a general purpose in systems that may be quite complex. In many cases the signal changes have come from laboratories with broad purposes, with many and diverse biological models and an interesting mix of scientific personnel. Most of these characteristics can be developed in large groups or in intimately interacting groups of smaller size. In either case, the resources required for an effective effort are quite broad.

There is probably no single lesson to be learned from these exciting developments that has relevance to the administration of scientific organizations other than the importance of providing for such intimate interaction within the operation of the institution when this is possible. The effectiveness of an individual scientist and the quality of his endeavor at a fundamental level may have little dependence on the arrangements within the institution. The effectiveness of his work is frequently due to the operation of a number of "invisible colleges." In such a situation the development of parallel activities and those in the more applied fields are not then the particular responsibility of any one institution, they are more the result of the random operation of a set of forces within the mechanics of science itself.

But the problems for the institutional management are still quite clear. In the case of a biomedical research enterprise, broad problems in medicine can be supported as a collection of discrete scientific activities pursued as ends in themselves; or resources can be allocated in a fashion that provides a more purposeful setting for the interaction of some of these scientific forces within a limited number of selected program areas.

Which is the wiser view. It is likely that the wisdom of an institution will be most manifest in its ability to select the areas which will benefit most by each method. Most certainly, many require some organization is only to provide the biological resource; some of these will benefit by a joining together of several groups in a common effort; other areas may not profit by such arrangements.

This section probably does not warrant any summary treatment - at least not of a substantive nature. The material discussed reflects more of a point of view concerning the varied opportunities in the biomedical field than a simple statement of what it is important to do. Then also, it reflects the view that the major problems suited for medicine and its related institutions are complex, and that most would profit by some consideration of order and organization in the allocation of resources with a clear understanding of the purposes to be subserved. It states that some of these should be stated in social as well as scientific terms; but there are other types of activity which should be viewed as parts of broader programs, the individual pieces of which acquire purpose only when the whole is viewed within the far reaches of science. Finally, it reflects the view that the excellence of an effort and its importance is not derived from the level (i.e. fundamental, applied or developmental) at which it is pursued. Fundamental research can be trivial; applied and developmental work revolutionary in its impact on science.

An institution should have a mix of programs when viewed in this general manner; it will profit by few programs with broad resources, than many which are inadequately supported; its reputation and its character will reflect both its purposes and the intelligence with which these purposes are pursued; but purposes it must possess if it is to have character and these must be well understood.



## V

## Some Program Proposals

This section includes a brief discussion of several considerations pertinent to the planning of further University development. Then a series of program proposals are made and each briefly discussed. Each proposal has fundamental science as its base but includes the application of new knowledge to a broad human problem. Taken as a group, they are examples of the type of program development that is both possible and desirable. The proposals may have as their major utility the presentation of a point of view that can serve as the basis for general discussions. Nonetheless, each proposal is believed to be reasonable, to have a sound base in existing science and if implemented, would benefit the University.

## General Considerations

Institutional planning is a process, which to be effective, must include the development of proposals which are quite explicit. However, the process of planning is complex and complicated. Proposals which suggest new dimensions for The University should be made with the view to evoke discussion of basic institutional purposes; not as a series of propositions easily converted into a blueprint to guide executive action. The process of change can be exciting or dull; and resented or accepted by the intellectual community depending, perhaps, less on the substance of change than on how this is effected, and the resulting influence on the scientific environment of the institution.

In the planning for institutional development there is obviously an overriding consideration. This relates to how major program innovation is likely to influence the character of the institution over the middle and long range period. Generally speaking, it is difficult, and usually not desirable to "turn an institution around" except in the case of institutions that have run out of a mission or when its program content is judged to be inadequate. Such circumstances may be particularly important in the review of mission oriented agencies of an official or an industrial nature. They do not usually obtain for educational institutions except where senior appointments over a decade or so have been unfortunate, whose resources for modern science are inadequate or when it is clear that a new dimension of science would be advantageous to the institution. The first two of these three characteristics do not obtain for the programs of The Rockefeller University.

The prospect of further program evolution for the University, can be in the light of changes in the nature of its programs and changes in the prospects of science since the last systematic studies in 1952. The review should examine the basic program and the propositions which were held to be determining for institutional development at that time. Were the same type of review undertaken today, would these same propositions be given equal weight as a basis for change as in the earlier period. Viewed in this light, most of the principles were obviously sound, though the details of others would probably be stated differently today.

In this view, program change and the modification of institutional objectives are viewed within a continuum of program evolution subject to periodic study by administration and faculty alike. Such an institutional review required no formal mechanisms in the earlier times. Programs were smaller, less

complicated, and fewer in number. The program resources were largely derived from endowment and support of the entire enterprise was at a much more modest level. Systematic program review was both possible and effective incidental to the annual consideration of budgets, and the turnover of institutional staff was quite low. It was possible, under those circumstances, for the objectives and programs of the institution to be easily comprehended, without recourse to formal reporting techniques, by an interested senior group of the faculty, the Director and The Board of Trustees. It was further possible for programs to be modified almost imperceptibly and progressively within a body of a slowly changing science.

But those circumstances no longer obtain in the University: nor do they in other settings where research is pursued as a primary institutional objective. Also, contrary to common comment, changes that are increasingly apparent in research organizations relate less to the origin of research support than to the size, complexity and substance of the programs, to the pace of present scientific discovery, and in the magnitude of the resources now necessary for a productive enterprise. In the case of The Rockefeller University, these changes have had a particular impact due to the rapid evolution of the biological and clinical sciences during the past two decades, and the disappearance of the hard barriers that heretofore separated the biological from the behavioral sciences. These changes are fundamental and have largely occurred since the last major review.

Considering these happenings, it is appropriate to pose questions, the answers to which will have immediate impact on the direction of program development.

The first relates to the general purposes of The University. Should The University continue to consider itself a specialized university, the programs of which will continue to emphasize those aspects of science which have particular relevance to the human in both health and disease. One must be quite explicit in developing an answer to this question since in the final analysis all science has relevance to the human species, the betterment of his existence, an improvement in the circumstances of living and his understanding of both himself and the world about him. The question is more simple and more blunt. Its major thrust concerns whether the University will continue to emphasize objectives with a medical connotation in the forefront of its planning; and whether it will develop its more fundamental programs in a fashion that provides a sound science base and a lively scientific environment for the pursuit of other activities of a more applied nature; and whether ample provision will be made for the latter programs that have direct relevance to an understanding of human development and the maintenance of health as well as the understanding of disease, its prevention, amelioration and cure.

In arriving at an answer to this quite fundamental question it must be understood that concepts of medicine have been considerably broadened, since the establishment of the Institute at the turn of the century, and importantly, since the examination of the Institute in the early fifties. The biomedical sciences now encompass the broad application of information from the behavioral as well as the biological sciences for the betterment of man, the phenomenon of human development, and the impact of an increasingly hostile environment on the human within broad ecological considerations. The major question relates to the extent that "health" and "medicine" are a major

directive force which will continue to be dominant in institutioanl planning - an answer to this question cannot be satisfied by disucssions more characterized by sophistry<sup>1</sup> than clarity.

The second question relates to some of the procedures The University may find useful in the fulfillment of its purposes. As indicated earlier, the development of any broad field is largely dependent upon the random forces within the dynamics of a lively science. However, it is frequently possible, as a matter of institutional policy, to facilitate the interaction of discrete groups within a broader program with general but quite explicit purposes.

An informational system; importantly, and in either case, it is likely that a more formal system of program examination is needed by The University for the provident expenditure of the funds available. It is likely that The University is of a size and complexity that requires an informational system that minimally will provide for the submission of relatively simple annual scientific reports by each of the senior faculty members. Each such report could reasonably contain in summary form:

- A brief account of activities during the preceding year.
- A projection of the direction of program during the coming year within middle range (perhaps 5 years) expectations.
- The current distribution of personnel and resources together with an estimate of their adequacy in relation to further program development.
- A brief discussion of collaboration with other scientific groups (within and external to The University) which may have influenced the course of development and the desirability of undertaking collaborative activity in the future.

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<sup>1</sup> Sophistry - deceptively subtle reasoning or argumentation - Webster.

The report might also contain the statistics of the operation relative to dollars expended, sources of support, and personnel changes. The bulk of this information can be supplied from a central source.

Such a reporting system would have many uses for the administration. It would provide a firm factual base for a consideration of the operation by the senior faculty, the executive officers of The University and its Board of Trustees. In that the assembled reports would be highly substantive in nature, they would be useful for planning purposes and in the allocation of resources. Such a set of reports are an essential for any reasonable expansion of the activities of The University. Quite apart from the utility of such information for internal use, The University must have a more factual account of the ongoing activity if serious consideration is to be given The University by prospective donors.

Actually, an informational system such as is proposed, is an essential for the prudent management of the resources available quite apart from the utilization or resource allocation as an instrument of policy in the evolution of new institutional programs. An informational base is always both essential and important for the allocation of resources in any situation not characterized by unlimited funds. The point to be emphasized is that the informational base must be sound if the intellectual community as a whole is to reap the greatest benefit from the resources available. The fact that The University receives approximately 40 percent of its support from sources other than endowment makes such a factual basis for programming all the more important, if the overall enterprise is to achieve the long term stability essential for a productive program.

### Program Proposals

Several programs are proposed for initial consideration. Each would add a new dimension to the intellectual community; each would require new physical resources; each would result in new operating relations within the metropolitan community; and each has as its end purpose the solution of a set of human problems. Consideration of these problems may be helpful in the broad definition of institutional purposes.

Research in reproduction. A significant program in this area can only be proposed in a document such as this in general terms; the specific elements deemed to be feasible for a single institution will be determined largely by the resource ultimately developed, its location and the relations which may evolve with collaborating institutions.

A comprehensive program would entail both basic and applied investigations in the behavioral, biological and clinical aspects of the entire range of reproductive phenomena including: (a) developmental aspects of puberty, including, for example, such problems as precocity, delayed puberty, abnormalities of gonadal differentiation and psychological aspects of adolescence; (b) adult sexual phenomena including, for example, mating, conception, contraception, fecundity, infertility, the climacteric, and psycho-sexual phenomenon generally; (c) pregnancy and such related aspects as spontaneous and induced abortion, complications of pregnancy such as toxemia and extopic pregnancies, and maternal mortality and morbidity; (d) perinatal and early post-natal phenomena with emphasis, for example, on fetal loss, prematurity, congenital abnormalities and the tetralogical problems related to prior exposure to physical and chemical agents.

Needless to say, an institutional program would be more modest in coverage and could conveniently cover the period of family planning, pregnancy and early development of offspring. Such studies should be integrated with subsequent observations on the psychological and somatic development of the offspring. However, these latter efforts would be more feasible outside of a reproduction research program proper, but could be included in related programs such as have been proposed below for the behavioral sciences.

Basic investigations in reproduction would entail work with a number of animal species as well as with the human subject. There is a growing skepticism as to the clinical significance of reproductive phenomena observed in the rodent and in other lower forms. Accordingly, there is greater need for emphasis on primate studies. This shift to a major emphasis on the use of primates in animal studies imposes logistical and budgetary problems of major administrative importance. These are especially burdensome in a crowded urban setting. Otherwise, the usual facilities and resources for biomedical animal studies would prove adequate.

The clinical studies outlined above would entail many special arrangements in order to blend the complex service requirements with the research function. Experience has shown that primary clinical control is essential to sound investigation on the human subject. No existing care facility now catering to a broad range of problems in human reproduction provides sufficient clinical control to serve as an ideal focus for the proposed research program. There would be needed a new type of community-based facility with suitable related in-patient resources. Both would require proper full time clinical and research personnel. The administrative arrangements would be such as to provide optimal clinical care as an adjunct to the primary research function.



A favorable setting for such a facility might be in a newly developing community health care program which services a mixed socioeconomic population. Two such programs are now in planning; one by the Roosevelt Hospital, the other by the French-Polyclinic group. A model laboratory clinical research center can probably be incorporated within the broad planning for these enterprises. It would then be quite feasible to provide for both long term and short term studies as a cooperative extension of either of these programs.

In theory at least, such a research function could be grafted on to a well planned and properly organized pre-paid comprehensive medical care system, including both in-patient and out-patient resources, together with a staffing and administrative pattern which would allow for a high degree of clinical control. However, the prospects for such a program are not good in the metropolitan area.

Admittedly, many acceptable studies are presently conducted in various centers providing obstetrical, gynecological and family planning services. For the most part these are short term, highly specific investigations with relatively poor follow-up and somewhat dubious records. For the most part, such research yields highly circumscribed data and provides little over-all comprehension of human reproductive processes.<sup>1</sup> With a rapidly changing moral and legal basis for human conduct in this area, even the most rigidly devised and carefully executed studies are fraught with difficulty. The development of resources and programs in these broad areas which will yield comprehensive and reliable data under conditions of optimal clinical care on a sound community basis presents an enormous challenge.

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<sup>1</sup>An exception to this may develop in newly planned studies at the Columbia Presbyterian Hospital Center. As best one can gather from informal enquiry, a new center will emphasize the family planning process and there already exists an activity in the area of child development. These are not planned as a single enterprise.

For example, most of the antifertility agents in current use are attended by a variety of biological phenomena which can be grouped under the heading of continuing pseudopregnancy and originate in a modification of the operations of the endocrine system. These agents directly influence ovulation and implantation, but the actions are also reflected in modifications of water and electrolyte balance, in changes of mood, and in modification of clotting mechanisms of the blood. They also produce cellular change in tissues that are common target areas for carcinogenesis. Despite their practical importance and general use, these agents have not been studied either in animal model systems or in man in a definitive fashion. Qualities of safety and effectiveness have rather been assessed by the net results of massive field trials. It is unlikely that wholly new agents will be as easily introduced in the future as in the past. Equally important, the bulk of the commonly used antifertility agents group around a single type of biological activity (i.e. progestational) leaving the many other phenomena of fertility, fertilization and implantation more or less unexplored. In consequence, the field continues to be open to innovative exploration, an essential of which is a more definitive understanding of normal processes.<sup>1</sup>

Importantly, the study of the physiology of fertility and its control is only possible within a setting that encompasses the entire gamut of services that are essential for family planning; including genetic counselling and the optional termination of pregnancy. But the associated services themselves provide broad investigational opportunity.

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<sup>1</sup>This area of early human development is one of those selected for extensive development by several units of the federal establishment.

Genetic counselling is in the early stages of its development. Even so it now requires resources for chromosomal analysis and metabolic study of cell clones derived from the developing fetus. There is thus available rather unique biological material for the exploration of many aspects of human genetics and their reflection in metabolic phenomena. The manipulation of the genetic substance, including a repair of genetic "defects" will continue to be a speculative though interesting enterprise. Meanwhile, developmental work is required to convert a series of research procedures into routines available for more general use.

Then too, since the termination of pregnancy is now optional, the opportunity for systematic study of the biochemical and biological phenomena which attend early pregnancy are open for reexamination within a context of timed human pregnancies.

The complex problems associated with fetal development are equally obvious. The simple morphology of development has been the primary concern of anatomists and embryologists since time immemorial. More recently, it is possible to consider development from a substantially broader point of view. The extraordinary changes in the biological systems which attend early development when viewed as the result of the sequential operation of the cell information systems bog the imagination, but an exploration of these phenomena must be begun.

Research in the development of human behavior. Studies in this area can be most rewarding in the immediate and middle range future. This is in part because of the deep insights that have been developed on the consequences that attend the early environmental experiences of the new born, in part because of the demonstrated influence of the early years on the characteristics of later intellectual development, and in part because of an increased capa-

bility to provide bridges between the biological and behavioral phenomena that attend human development.

These features of human development with their broad base in comparative studies are particularly suited for consideration by The University because of already existing excellence in several related fields. But it is doubtful whether these scientists can take advantage of the general opportunities unless there is an expansion of staff in several critical areas and unless more suitable clinical and animal resources can be made available.

Some indication of the specific nature of work that can be undertaken as an extension of ongoing programs are contained in recent proposals for studies of "Human Development and Learning" and "Primate and Animal Studies of Behavioral Development." These proposed studies are quite specific and merit favorable consideration in their own right. However, they would benefit from a broader statement of purpose directed toward the understanding of the biological and behavioral determinants of human development.

For such a group of related studies to be effective, small groups of children alone and in association with elements of the family group would have to be available under highly controlled environments during major portions of the early development period. These observations are not easily made in the conventional experimental school; novel arrangements are necessary; and it is necessary to include the study of special groups of children in settings different from those obtaining in a metropolitan environment.

The basic requirements for most of these studies is a physical resource and a program that maintains a systematically ordered population group covering the period of development to be studied, assorted biologists and

behavioral scientists with suitable motivation who are grouped around one or more of the major areas of exploration to be undertaken and the broad back up of a number of animal model systems, these to include primates.

The clinical expression of these resources are now conventionally found in well baby clinics, pediatric departments of medical centers as well as in experimental educational settings. Most of these resources are organized quite separately one from another and are primarily suited for the delivery of specialized medical or educational services. The opportunistic superimposition of investigative activities upon such service activities are too frequently ad hoc in nature. As such, the services do not provide an adequate central resource for really critical research.

But, it is possible to provide for a more suitable clinical setting and such an organization could provide quite adequate health services. A suitable population group, when properly organized, would require a mix of clinical care personnel and an adequate investigative staff and suitable back up resources. However, an important point must be made. It is unlikely that any population group desired for study can be held together for an adequate length of time unless a set of related health services of high quality are provided as an essential core for the program.

An inordinate amount of space, in this discussion, has not been given to these aspects of early human development. There is no doubt that the environmental circumstances attendant on this early period are as important in the determination of adult capability as is the inherited genetic capability. The initial years largely complete most of the biological and much of the fundamental behavioral characteristics upon which subsequent development into adulthood will depend. It is true that this obtains for the more general biological functions such as body size, etc. More important though,

is the conditioning of the quality of the cognitive faculties, the patterns of perception, learning, speech and language which may be difficult to modify during subsequent development. Our present systems of child rearing now pays particular and detailed attention to the biological needs of the developing infant and the young child, with little attention to behavioral and intellectual development prior to the child's entrance into the formal educational process. By this time, much that is not reversible has already taken place. Present information does not provide firm guides to action, only an appreciation of the importance of this period of growth.

Substantial benefit would derive from an association of these programs with some of those considered under the heading of Research in Human Reproduction. Both types of study require access to a general population with a mixed cultural background, the ability to select small samples for special study, and service arrangements which would tie family group to a study program for long periods of time.

All these could be arranged within the operations of a comprehensive community health program, particularly one that encompasses the study of human reproduction from a broad point of view. It is further pertinent to point out that the animal resources for the two general types of study have much in common. These would require fairly extensive control of the environment of a number of animal species including primates. Both sets of studies would require varying degrees of control over both the behavioral and biological characteristics of the environment.

The suggestion emerges from these considerations that The University might well consider the possibility of establishing a subdivision of its activities directed in a purposeful way to the phenomena attendant on Human Development. This would be a major university enterprise important

in itself but with broad interaction both with the metropolitan community and some of its institutions of higher learning.

Research in Atherosclerosis is another area that might be considered for emphasis as part of the further development of The University. The general nature of the opportunities for research in atherosclerosis was briefly discussed in Section IV. Advantage could be taken in such a development, of the existing commitments of University scientists to a number of associated problems that relate generally to the disease. But the scale of these activities is too small for them to be considered a major university program.

The importance of medical problems associated with atherosclerosis is reflective of the fact that the major problems in "medicine" today are in the chronic disease area. Many important studies of chronic diseases can be conducted in the conventional hospital setting, particularly when the studies are directed toward acute phenomena which appear intercurrently within the longer term progress of the basic illness. But the study of the disease process itself requires the long term study of individuals with disease against a backdrop of a developing understanding of the normal operation of the systems particularly involved in the disease process. Furthermore, when the special disease under study is due to an underlying disturbance which can be caused by more than a single cause and the morphology of a system limits the nature of the phenomena attendant upon the development of overt disease, then the disease models which can contribute to an understanding of the pathogenesis of disease are numerous. This set of complex requirements has tended to limit the effectiveness of programs in many areas of chronic illness in the conventional University Hospital and this is even more true for atherosclerosis than for many other disease conditions.

Problems of this order of complexity should serve as a special challenge to medical research organizations because of the selectivity they can exercise in the subject material undertaken and their ability to provide for the back up research that is essential. Contrary to the University Medical Centers, the research oriented institution does not have the need imposed upon it, to provide for a complete array of specialty groups for both medical education and specialty training. Furthermore, the urgencies of these needs in the conventional medical center setting tends to occupy so much of the faculty time that their activities are generally hospital centered. To date, medical school faculties have been quite unable to participate in the development of broadly based community programs, a primary purpose of which is the conduct of research. These institutions are under such heavy pressure to provide for medical service programs as ends in themselves and for the progressive modification of medical service systems, that they have little opportunity to utilize the new arrangements for research purpose. Research oriented institutions need not suffer such distractions.

Apart from these organization considerations, the undertaking of a major program in the field of atherosclerosis has much to recommend it as one of several in the chronic disease area that might be given high priority by The University. Program development can be based on an extensive body of information that relates to lipid metabolism and lipid transport. The study of these systems in diabetes, in obesity and in what would appear to be uncomplicated atherosclerosis would provide information on the interconnections of a series of important disease entities, and the consequences of these diseases to the target organs such as the retina, the heart, the kidney and the Central Nervous System.



Such a centrally important disease process warrants attention in its own right. Additionally, as the result of recent decisions made at a national level, more than ordinary financial support will likely be available despite an almost certain continuation of constraints on the federal support of research.

Looking to the middle range future (5-10 years) it is likely that our knowledge of this disease will develop rapidly. This estimate poses a serious problem for the individual investigator. For a productive program it is likely that he must associate himself with a national program that provides tight coupling of his own activities with others in a collaborative effort. Alternatively, an institution may elect to emphasize research in atherosclerosis as an institutional effort of major magnitude. Such an effort would represent a substantial challenge. The challenge derives from the fact that the exploration of the disease with suitable leadership at both the laboratory and clinical level can be guided in a fashion that has a high prospect of success and the achievement of a leadership role in a program of obvious national importance.

Should this area be considered in the further development of The University's programs, then it should be considered in relation to the studies on human reproduction and human behavior discussed above.

A comprehensive program in atherosclerosis has as an essential, the availability of several controlled population groups. One must be of substantial size for random sampling and for control biological studies. Then there must be smaller groups such as are contained in specialty clinics with well documented patients manifesting systematic disorders of a metabolic nature. Particular attention in these groups can be given to the phenomena

attending diabetes, heart disease, obesity and other groups at high risk, including patients with familial metabolic defects. Such patient populations can be grouped around any one of several clinical settings which have as their purpose the provision of comprehensive health care, a common requirement for the study of human development noted above.

Supporting these clinical resources, well instrumented biochemical and biophysical laboratory facilities of more than ordinary volume capability must be available. These would be needed for the repetitive study of the biological systems believed to be important in the genesis of the metabolic disturbance and to monitor changes purposely induced. It is obvious from this brief consideration that for such studies to have the opportunity for success, there must be a broad institutional commitment to pursue the problem of this disease in depth, in breadth and for a long period of time.

Within such a view the present Rockefeller Hospital would continue to be a critical resource for the performance of the detailed studies not generally suited for the conventional clinical setting. But, as with the studies on human development, the primary clinical resource would be the community population for the study to have reasonable prospects for success.

Other areas of science will not be explored in this presentation.

Those given summary treatment can be taken as typical examples of problems that would profit by expansion of resources, that couple laboratory and clinical resources such as might be possible in association with one or more health care systems.

But a limited examination of a number of other areas of University activity show many to have a feature in common. This is an ability to make the present activity more significant through an ordered expansion.

As another general characteristic of a number of activities reviewed, many would profit if expansion is provided in a fashion that would facilitate contact of the activity with other ongoing activities with parallel objectives. These observations do not derive from a comprehensive survey of the variety of programs now contained within The University. Such an examination, to be undertaken, would have as a requirement a more effective central information system than is now current.

Further, the present study has been limited to some activities that are medically oriented, more so than is generally true of many of the biologically oriented programs of The University. Nonetheless, the study should not be taken simply as special pleading for a broader orientation of University activity toward programs of medical and consequently of social interest. Rather they reflect four general and separable points of view.

The proposals in the field of human development have the possibility of achieving two scientific and one organizational objectives.

- The time is particularly ripe for the biological and behavioral sciences to join in common cause with the view of clarifying our understanding of the influence of genetic as well as pre and postnatal environmental factors on the ultimate potential for biological, emotional and intellectual development. Studies in these fields can have critically important impact on very general concepts of child development and the relation of these to the conventions governing the rearing of the child and the early stages of the educational process.

- The studies on human reproduction proposed for consideration can give prominence within the programs of The University to many scientific activities that are equally critical to the problems of population and population control, a general problem of substantial social import.

- From the standpoint of organizational considerations, the complex of study program proposals in these general fields of human development provide a natural bridge for redeveloping more intimate working relations of The University with the Rockefeller and other major foundations with long term interests in these areas. They would also provide a productive working link with a population segment and with some of the intellectual elements of the metropolitan area.

The proposals covering the field of atherosclerosis reflects the view that the state of knowledge of this process permits the statement of some general working hypotheses that warrant definitive exploration. The complex of disturbances which lead to the evolution of the disease are important, as are their expression in overt disease of vital target organs.

But, more importantly, each study emphasizes the view that the opportunity for striking advances in medicine has shifted from phenomena that can be observed over short periods, to phenomena that can only be productively examined over long periods. The medical community has found it difficult to adapt to the new situation even though both educational and research opportunities are influenced equally. In such a situation, the hospital and its laboratory resources become ancillary to the study of population groups over long periods of time. Consequently, most chronic illness is not suitably studied within the confines of the usual specialty clinics of The University hospital. Other arrangements are essential and these will be most effectively developed in association with the comprehensive health care systems which are now beginning to develop. But, if these are to be useful for both research and educational purposes, then wholly new concepts in their organization must emerge. It is believed that the clinical needs for sound studies on human

development and on atherosclerosis would be helpful as guides to the overall design of such a resource. The scientific opportunities are obvious.

Not related to the specific studies proposed, but more to the general area of concern for The University is yet quite another consideration. It is believed that the present Hospital of The Rockefeller University is important but only suited for a limited type of study. Further, to provide a more general facility, such as could produce a capability for intimate coupling of clinically and biologically oriented scientists within a common environment, is prohibitively expensive even at the current program level of medical research. Were this done, it would still not provide a suitable environment for the comprehensive study of most chronic disease. Other arrangements are required. But perhaps of fundamental importance is the conviction that the present medically oriented groups and the resources available to them are inadequate for a vigorous program of medical research such as would provide both balance and opportunity to the more biologically and behaviorally oriented scientists of The University.