ANNUAL REPORT
OF
PROGRAM ACTIVITIES
NATIONAL INSTITUTES OF HEALTH
1957
NATIONAL INSTITUTE OF MENTAL HEALTH

NATIONAL INSTITUTES OF HEALTH
PUBLIC HEALTH SERVICE
U. S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
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INTRODUCTION

There are relatively few resources around the world for basic research in the mental and neurological field. Problems that need solution are staggering. The present overdemand for medical services cannot be diminished except through fundamental advancement of concepts. With few resources and immense problems we need to make especially effective use of what is available. How to do this? Simply stated, it is by giving encouragement and stimulation to the most creative scientists interested in fundamental problems in this field and by providing that support by which they can be most effective.

Unfortunately, there is no simple recipe for achieving this goal. Something worthwhile may be accomplished, nevertheless, by setting forth new and compelling reasons why it is desirable to pursue research basic to neurology and psychiatry. And it may also be helpful to make even a preliminary enquiry into what is the nature of scientific creativity.

All of the old reasons for examining the functions of the nervous system still exist. Among the most important of these has traditionally been the desire to know on the part of those involved in research—pure intellectual curiosity. The nervous system is concerned with those things that mean the most in human life. Man's own curiosity about himself as a perceiving, thinking being can only be satisfied by pursuing the anatomy, physiology, biochemistry, pharmacology, psychology, sociology and allied disciplines relating to the brain. Always there has been a pressing need to know in order to solve clinical problems. This reason has generally been uppermost in the minds of those who have provided support for research.

THE URGENCY OF BRAIN RESEARCH

It needs to be emphasized that the brain is an instrument for social as well as physiological integration. The peoples of all nations are in need, rather suddenly, of the means to understand and cope with a myriad of problems relating to
perception, memory and emotion and to learn how to become more constructively adaptive as interdependent individuals. Social and technological revolutions are hurtling us, as one of the authors of the recent Gaither Report succinctly remarked, "right into the mouth of Hell." It remains to be seen whether we can find ways to maintain freedom where it exists and to establish it where it is lacking. In the meantime, some kind of world government under law is called for to forestall a global catastrophe that now seems so probable. The shield of our republic will depend more and more upon the creativity of human social thinking and less and less upon direct instrumentalities of war. The latter can only provide a gap of time within which certain crucial social adaptations must take place.

At the root of the matter are as yet unsolved problems relating to the perception of actions and of shibboleths, the translation of ideas, the momentum of traditional concepts, the adhesive behavior of groups, the communication of ideals and goals. Many scientists have confidence that these problems can be solved, given time and effort. Our country is presently buying time; we can undoubtedly improve our effort. Ignorance of basic mechanisms acts as a handicap to current attempts to meet these problems. There may be short cuts, but few are evident. We have to learn how signals enter the nervous system, how they are distorted by concurrent and antecedent events, how they relate to mechanisms of reward and punishment and emotional expression, how learning occurs, and what are the limitations of our mnemonic and behavioral response systems. These mechanisms have their anatomical, physiological, chemical, psychological and sociological manifestations. What more interesting or important labor than to be involved in the unravelling of these mysteries?

There are bases for optimism in relation to finding solutions to these difficult problems:

1. Creative thinking will undoubtedly be more and more deliberately cultivated within the government. In the past, creativity has not been favored in relation to social or political action; instead, the emphasis has been on stability and continuity of the familiar. Creative talent for several hundred years has had to find individual, usually unsupported, expression through music, literature, art and science. Recently, and with spectacular results, creativity in scientific endeavors has been supported by governments and industry to the enormous material advantage of mankind. The object of this lesson appears too clear to be missed in relation to man's psychological and sociological needs. A more creative approach to governmental issues will invite answers to these problems; one can already discern the trends. Leadership in government will hopefully become less like steering the car of a Juggernaut and more like deliberating the most advantageous moves in chess.
2. Progress in fields basic to sociology, psychiatry and neurology is rapid. There is a natural tendency, at any given moment, to imagine that science is in a pretty comfortable state; the directions are obvious for a great deal of work to be done just to clear up "loose ends." Nevertheless, a glance over one's shoulder just a few years back elicits a rather giddy sense of speed of events in any branch of science. Physicists have in the last year had to throw away three of the most fundamental principles of the universe. Although less spectacular, revolutionary changes are also taking place within the psychological, neurological and sociological sciences. Twice in the past year the Basic Research Program has been asked to prepare reviews concerning recent advances in areas of our interest; it has been genuinely surprising to take notice of the speed of overall conceptual growth. Furthermore, discoveries among complementary disciplines now appear to dovetail in ways that could not have been anticipated even three or four years ago. Resources of the National Institutes of Health and of a number of other governmental and private agencies have played an important part in the achievement of these advances.

3. Progress in these fields will be even more rapid if we deliberately cultivate the best opportunities for creative contributions. The most favorable utilization of creative talent is not a trivial issue. It needs to be thoroughly and thoughtfully examined. Albert Einstein wrote: "It is, in fact, nothing short of a miracle that the modern methods of instruction have not yet entirely strangled the holy curiosity of inquiry; for this delicate little plant, aside from stimulation, stands mainly in need of freedom; without this it goes to wreck and ruin without fail. It is a very grave mistake to think that the enjoyment of seeing and searching can be promoted by means of coercion and a sense of duty." The most fruitful achievements by creative persons apparently require three things: personal mastery of a province of science, personal discipline and personal freedom. All three factors need to be of a high order.

4. The brain is a very incompletely exploited instrument for survival. The nervous system is an evolutionary product that has played its role in human development and survival just as have teeth and claws. But we can expect from it much more constructive and creative possibilities. An adequate utilization of present knowledge in areas of our greatest national need has not been attempted in any systematic way. As further insight emerges, we can expect to better understand human capabilities and limitations in perception, memory and communication and to learn ways of engaging reward-punishment and emotional mechanisms along relatively more constructive channels.

As Professor Percy W. Bridgman, the eminent physicist at Harvard, has been careful to point out, all knowledge of the universe is dependent upon the level of understanding of
neurophysiology and psychology; this is essential for the interpretation of sense data and for certain logical, mathematical and verbal operations that are involved, many times in a limiting way, in the formation of concepts of physics. It was in an analysis of comparable instrumental operations involved in the measurement of length and time that Einstein discovered certain non-common-sense aspects of the universe which form the basis of special relativity. As we learn more about human perceptual and conceptual processes, we will gain insight not only into ourselves but into more general features of the physical world as well.

We consider that the public need for basic knowledge in all fields relating to the nervous system is one of the most urgent and worthwhile as well as fascinating areas of scientific endeavor. Warren Weaver, Vice-President of the Rockefeller Foundation, recently said "in the realm of human behavior including all those social, economic, and political aspects of individual, group and mass actions which constitute the social sciences . . . progress in understanding, and eventually in controlling, these phenomena is just as sure to occur as is progress in understanding the cell. We must not be impatient or critical—surely not contemptuous—of the tentative and fragmentary nature of the successes to date . . . the first exciting invasions into the world of the mind and behavior."

We would welcome an objective disinterested examination of the dimensions of these issues; the urgency of our national need for new basic knowledge relating to the brain and its activities; the potential value of current research; the ultimate promise of basic research in this field to public problems; and a consideration of all of these evaluated findings in relation to the total research endeavor being supported by the Federal Government.

CREATIVITY

Problems that resist solution may be insoluble, yet, if you will believe the history of science, it is more likely that the means of solution being attempted are inadequate. Certainly, in the absence of fresh insight, sheer devotion is powerless to do more than refine what is already known. It takes a creative person to turn aside from established schemes of consciousness and to seek out that which can lead to something more fundamental. Occasionally the entire framework in which a problem is presented needs to be creatively reformulated. A theory can be tested by experience, but there is no direct path from experience to the setting up of a theory.
A more adequate understanding of nature cannot be achieved in the abstract; it must be brought about through the consideration of materials with which the scientist is already familiar. Even the most gifted and energetic person must have achieved a certain mastery in the field of his pretended accomplishments. He must have a keen sense of what needs to be done to solve a given problem and a sufficient skill to do that. He needs not only carry out a program of thought and action at the limits of conception, but he must follow through by communicating in a clear way his new level of understanding. His scientific achievements in the end represent only a better approximation--the end can never be a statement of finality.

Highly creative ability in any field of endeavor is so relatively rare and little understood that it is usually suspect. Every new step in the development of an idea is likely to seem alien and eccentric. One who would be creative must deliberately encourage the imaginative manipulation of ideas that have only tenuous credentials. Yet the mechanism of creative scientific accomplishment are not under any satisfactory degree of voluntary control. It requires from the scientist a thorough understanding of the problem, discipline and hard work, but also something more than that: creativity cannot be squeezed out of paste is extruded from a tube. It needs the exercise or "release" of some nimble elements of combinatory play of imagery in a form that usually precedes logical construction into words or symbols. Moreover, and this is a feature of the greatest importance, the process is easily disturbed or put off. Even too urgent a desire to arrive quickly at logically connected ideas may foreshorten a conceptual advancement in the making. Because of this, discipline of the creative process should largely arise within the individual, or be provided by example.

There is another feature of creativity which is less clearly appreciated, that of nonconformity. As Ben Shahn has recently written: "Without nonconformity we would have had no Bill of Rights nor Magna Carta, no public education system, no nation upon this continent, no continent, no science at all, no philosophy, and considerably fewer religions. All this is pretty obvious. But it seems to be less obvious. But it seems to be less obvious that to create anything at all in any field, and especially anything of outstanding worth, requires non-conformity, or a want of satisfaction with things as they are. The creative person--the nonconformist--may be in profound disagreement with the present way of things, or he may simply wish to add his views, to render a personal account of matters..."

"Yet, when it comes to the matter of just what kind of non-conformity shall be encouraged, liberality of view recedes. There seems to be no exact place where nonconformity can be
fitted in; it must not be admitted into the university curriculum--that would produce chaos. In politics it is certainly inadvisable--at least for the time being. It cannot be practiced in journalism... In science--least of all, alas!” Shahn goes on to conclude that "The degree of nonconformity present--and tolerated--in a society might be looked upon as a symptom of its state of health."

Important scientific achievements thus seem to depend upon the fruitful combination of a group of essentially positive factors; some of these relate to the competence, self-discipline and nimble imaginativeness of the scientist himself and others concern his surroundings. Research in laboratories of the Federal Government will surely progress in the sense of advancing the frontier. And the rate of advancement may be speeded up somewhat by administrative hustling or by providing additional money or personnel in a given field. But saltatory advancement of concepts--the kinds of change in point-of-view that may alter the entire character and direction of scientific pursuit, the kinds of advancement that may cut short years of striving--these are not likely to occur except where circumstances are especially favorable for creativity. In the long run, the reputation and credit of any laboratory will depend upon a few advances of this sort far more than upon the extension of studies that now seem entirely familiar.

AN INHERITANCE

A year ago when invited to participate in the Basic Research Program of NIMH-NINDB, I already had a high regard for the individual scientists in the Program and for their overall endeavor. The group, recruited and led by Dr. Seymour S. Kety, was widely recognized throughout the United States and abroad as performing outstanding research across most of the frontier of complementary disciplines relating to the nervous system. All this had been accomplished within five years. Despite Dr. Kety's heavy commitments to purely administrative efforts, he continued to pursue research; he perfected his theoretical treatment of blood-tissue exchange, extended his pioneering studies on human cerebral circulation and metabolism, and demonstrated a new method for determining local cerebral blood flow simultaneously in individual regions of the brain.

It is understandable that after such achievements, simply maintaining the Program in being could pall for Dr. Kety. Moreover, he needed to be relatively more free to accelerate his own laboratory research. He would also then be able to provide immediate leadership for a group that would undertake a broad-scale investigation of the "biology of schizophrenia." For these several reasons, Dr. Kety asked for replacement in his job and thereby established a precedent for rotation of this administrative office.
Before accepting so large a responsibility, it was natural to take a deliberate and hard look at the Basic Research Program. Close examination satisfied me and associates to whom I appealed for advice that the excellent reputation of the Program was entirely deserved. In addition to a feeling of satisfaction as regards the purposes and character of the Program, I also felt a strong conviction that the United States Government should be supported by its citizen-scientists in every way they are able. Dr. Kety's invitation to join the Basic Research Program was not only flattering in one sense, it was also an opportunity for dedication to an important cause. Having completed a "Freshman Year" in this job, I can say without qualification that my regard for the Program and for Dr. Kety's contributions has risen still higher. I can scarcely measure the agreeableness that stems from respecting and liking every scientist in the Program: this is a continuing reflection of Dr. Kety's wise recruitment.

GENERAL COMMENTARY

During the last year we continued trying to recruit a Laboratory Chief for Neurochemistry. In succession, two very excellent men were invited. Each was keenly interested in joining the Basic Research Program, even though it would mean no increase in salary. When it came down to particulars, however, we did not have enough space. Each was willing to come at a sacrifice of their present considerable space, believing that some of this deficiency could be made up by the central and collaborative facilities of the National Institutes of Health. But neither could establish even skeletal programs within the number of modules we had available. Space discussions occupied us for months, but no adequate adjustment or construction possibilities appeared. The same contingency proved critical in relation to recruiting a Chief for the Section on Perception and Learning in the Laboratory of Psychology. Finally, we had an opportunity to develop the important area of auditory physiology and psychology, but again, space limitations were critical. It is gratifying to know that we could build with strength and that our Program is competitive on equal or even disadvantageous terms, but it is also obvious that space is our most precious commodity.

Limbic Integration. By taking advantage of Dr. Kety's foresight in planning for a Section on Brainstem Mechanisms which had never been activated, we were fortunate to be able to invite Professor Paul D. MacLean of Yale University to join the Program. Dr. MacLean's interests in psychosomatic mechanisms and his brilliant studies concerning the anatomy, physiology, chemistry and behavioral aspects of the phylogenetically older parts of the brain have attracted world-wide respect. At the time of our
invitation Dr. MacLean was on leave of absence from his university, spending a year of study in Zürich. He brings with him not only his own exceptional talents and the traditions of Professor Fulton's laboratory at Yale, but also the rewarding influence of recent visits to many of Europe's finest laboratories. The new section headed by Dr. MacLean is called the Section on Limbic Integration and Behavior. It is jointly identified with the Laboratory of Psychology and the Laboratory of Neurophysiology.

Graduate Students. The Laboratory Chiefs agreed that we should restrict the acceptance of graduate students to the best possible candidates throughout the nation instead of favoring scholars of the Potomac Basic. We now encourage suitable graduate students from any part of the country who wish to do thesis work in our laboratories. They may find this advantageous by reason of the opportunities to work with particular scientists, have access to special facilities and the interdisciplinary setting of the Basic Research Program and at the same time discharge their military obligation. The local preceptor would undertake the special responsibility of supervising the candidate's thesis and may if mutually agreeable become a member of the Doctoral Committee at the candidate's home university. The university faculty advisor would at the same time become a Consultant to the Basic Research Program and would participate in planning and supervising the thesis work here. The first graduate candidate participating in this plan is Dr. Stanley Glauser, a medical doctor now completing his thesis for a Ph.D. in Chemistry from the University of Pennsylvania. His local preceptor is Dr. Alexander Rich, Chief of the Section on Physical Chemistry. His faculty advisor is Professor Philip George, Research Professor in Biophysical Chemistry, University of Pennsylvania.

Research Associates. A Research Associates Program designed nearly two years ago was launched last July. The purpose is to provide two years of combined preceptor and didactic training in basic research to outstanding men who have completed an internship and who wish to continue in academic medicine. The didactic training is intended to supplement and extend in a more penetrating way the exposure to basic biomedical science provided in medical school. Four of the National Institutes of Health are participating in this Program. Seven out of the first class of fourteen Research Associates are being supported by the Basic Research Program, NIMH-NINDS. Scientists in the Institute of Mental Health are making a study of the aspirations and creativity of the Research Associates and of the impact of this training program on their career development.
Visiting Scientists. The primary objective of the Visiting Scientist program is to provide a mechanism for cross-fertilization of ideas and for collaboration between our Institutes and Universities elsewhere in this country and abroad. During the calendar year, we have enjoyed the association and profited from the scientific skill of some eighteen individuals participating in the Visiting Scientist program. Six came to the Basic Research Program from England, three from the United States (one of these was from Puerto Rico), two from Japan, and one each from Australia, Canada, Denmark, Germany, Hungary, India, Korea, and Switzerland. Six of the eighteen are senior scientists. We are fortunate that by mutual agreement four of the eighteen are immigrating to fill Civil Service positions in the Basic Research Program. One of the four received his papers during the year and has already transferred to permanent status with us.

We are very pleased that Professor H. W. Magoun of the University of California at Los Angeles chose to join the Intramural Research Program of NIMH as a Visiting Scientist during his sabbatical leave. He pursued research with Dr. John Lilly, Chief of the Section on Cortical Integration, and with Dr. Edward Evarts, Chief of the Section on Physiology, in the Clinical Program of Dr. Kety's Laboratory of Clinical Science. With Dr. Evarts, Dr. Magoun demonstrated that the recruiting response in cortex is modified by alerting reactions on the part of the animal. With Dr. Lilly, Dr. Magoun examined behavioral stop-start mechanisms in subcortical structures, mechanisms apparently related to pleasure, fear and sexual excitement. Dr. Magoun also attended courses in the History of Medicine at The Johns Hopkins University and Hospital and gave a few seminars and lectures at various universities on the Atlantic Seaboard. He was responsible for initiating the Anglo-American Symposium on the History and Philosophy of Knowledge of the Brain and its Functions which was held in London, July 15-17 under the sponsorship of the Wellcome Historical Medical Library with the cooperation of the National Hospital, Queen Square, and the Maudsley Hospital. This was reported as being the most successful and interesting international meeting of last summer. We would like to encourage the practice of other notable scientists as well taking sabbatical leave here at the National Institutes of Health.

ROBERT B. LIVINGSTON, M.D.
The Basic Research Program, NIMH-NIMHD, includes the following laboratories which are combined with Clinical Investigations:

Laboratory of Psychology
Laboratory of Clinical Sciences
Laboratory of Socio-environmental Studies

The summaries for these laboratories on the following pages include only those Sections in the Basic Research Program.

The overall summary for these laboratories is included under Clinical Investigations, pp. 33-56
This has been an active year for members of the Section on Aging and the specific research findings of the present year will assist considerably in outlining long-range research programs in aging. As in the past, research effort has been divided among projects employing animals and studies of the normal human subject. The work of Dr. Jack Botwinick and his associates indicates that there is evidence for a change in inhibitory processes and control functions that are involved in motor, perceptual, and mental abilities. This is an extension of previous experimental and conceptual work of the laboratory. Analysis of the data on over 59 human subjects with a broad range of psychological measurements is now in process of statistical analysis. It is expected that these results will be available for publication in the spring of 1958. Dr. Alfred Weiss who also participated in the studies of human aging is concerned with three areas: click perception, dual channel auditory perception, and delayed auditory speech feedback. Only the click perception data has been analyzed thus far. The data on click perception indicates something of the nature of the perceptual deficit which can occur in some older individuals. Older individuals have increasing difficulty as the number of clicks increases. However, response time does not differ for two age groups, suggesting that the relationship between response time and perceptual ability, or accuracy, is more complex than previously realized. As an outgrowth of a study on age changes in retinal potentials, a micro-electrode study of retinal and optic tract potentials of the cat's eye in response to light was carried out in collaboration with Dr. Robert Cohn of the Naval Medical Center by Dr. Weiss. The results of this study are now being analyzed. In another collaborative study with Dr. Conan Kornetsky of the Clinical Sciences Laboratory, it was found that chlorpromazine was without effect on delayed speech feedback while secobarbital markedly increased susceptibility of the subject to speech disruption with this method.

Dr. Edward Jerome has been studying age changes in rat activity, rate of learning, and ability to transfer in a series of ten, escape choice problems employing light aversion as the drive. Preliminary analyses of the yet incomplete results indicate that, although the older animals were somewhat slower than the young ones, the two age groups did not differ with respect to reaction to obstruction, type of errors, learning rate, nor ability to transfer. These results can be interpreted as impugning the hypothesis that impairment of learning ability and flexibility of behavior are necessary concomitants of a decay of biological organization with increased longevity of the organism. They are, on the other hand, consistent with the hypothesis that when apparent impairment of these functions is observed in human beings, or does occur in animals, it is due to experiential factors, e.g., absence of recent relevant practice, low motivation, accumulation or strengthening of sources of interference, or lack of familiarity with the test situation in general or in particular. These preliminary investigations are being extended.
Section on Aging (Cont'd)

Dr. Eugene Streicher has continued his studies of age differences in calcium of the brain. In all age groups, from one month to two and a half years, the calcium content of the rat brain is very variable. The two halves of the same brain often differ by 100 percent or more in calcium content. However, the values for the two halves of the same brain are more closely related to each other in the tissues of old rats than in young animals regardless of the level observed. On the basis of relatively few observations, it appears that the magnesium content of the brain is somewhat diminished in animals over two and a half years of age. From measurements on the magnesium content of brain from rats of different ages, it appears likely that, in contrast to the reports of other investigators, the magnesium content of the myelin sheath is relatively low.

Dr. William Bondareff has continued his studies of age changes in nervous tissues of rats. His electron microscope studies of spinal ganglia from aged rats conventionally fixed with osmium tetroxide, have resulted in the demonstration that the genesis of the lipofuscin (the so-called senility pigment) is not directly related to possible age changes in mitochondria. This work which has been published in the Journal of Gerontology emphasizes that pigment originates in the cytoplasm of old nerve cells in association with vacuoles of submicroscopic size and it is suggested that this process is associated with age changes in the golgi complex. In an attempt to further investigate the process of pigment particulates, tissues fixed by freezing and drying have been investigated. These investigations are currently being continued and some progress has already been made in the application of these methods to the study of submicroscopic cellular changes of aging nerve cells.

Mr. Joel Garbus has extended his studies reported last year on the oxidative phosphorylation of fortified brain homogenates to include studies using other brain particulate fractions. A preparative procedure was developed for the isolation of cellular particulates of high metabolic activity and stability. Oxidative phosphorylation, measured in mitochondrial fractions prepared by these methods show no decline with age in central nervous system preparations from aged rats. These activities are measured under ideal in vitro conditions, which may not pertain in vivo. It is therefore proposed to make similar measurements using less than optimum conditions, such as anoxia, limited substrate, etc., reproducing a less favorable cell environment which may be a factor in senescence. Collaborative studies undertaken last year with Dr. Eugene Weinbach of the National Institute of Allergy and Infectious Diseases will be continued to study other aspects of cellular metabolism and aging.

The Section on Aging has continued to act as a coordination center of the research program on human aging in the NIH. At present this project is in the stage of analysis of data. Mr. Samuel Greenhouse and Mr. Donald Morrison are now actively developing high speed computer methods to intercorrelate the many variables from the different laboratories concerning changes in personality, cognitive and perceptual abilities, and physiological factors, in normally aging individuals.
Section on Perception and Learning

During the year Dr. Carlson's studies of the effects of LSD on the absolute visual threshold have been completed. The findings in man indicate a central effect of this drug in that the photopic threshold was raised significantly more than the scotopic threshold. Brightness vision in man undoubtedly depends to a great extent upon the cortex, and presently available evidence suggests that cone vision depends more on the complete integrity of cortical functioning than does rod vision. The presumed hallucinogenic effects of LSD were not found with the normal subjects used here. Psychotic and neurotic patients have shown evidence of an elevated visual threshold, however, so that this effect of LSD may constitute another point of similarity between the effects of the drug in normal humans and the manifestations of more naturally occurring psychological impairment. The absolute visual threshold was found to be raised more strikingly in the pigeon, although the effect is probably mediated subcortically in this animal. Another very interesting finding with LSD in the pigeon is an improvement in performance in a conditional visual discrimination task. The reason for this effect is not clear at the present time, but it may have a possible parallel in human performance. Under certain conditions normal subjects with LSD, anxious or tense subjects, and some schizophrenic patients seem to be better able to maintain directed attention and interest in what usually is a simple and tedious task for a normal subject. One effect of LSD may be to render the subject less susceptible to outside distractions and at the same time less able to integrate accessory cues into a unitary perception. Partly for this reason, the effects of LSD are being investigated on more complex perceptual tasks such as size-constancy and visual illusions.

Dr. Carlson has also continued his study of the Kohler theory of satiation in relation to neural processes associated with perception with a view towards using the methods developed for the study of basic processes of attention and short-term memory. He has also continued on the difficult technical problem of recording eye-movements electrically. The problem at present breaks down into three stages: (1) To work out the technical problems, which is the stage in which the work is concentrated. (2) To work out the methodology measuring psychological variables by means of eye-movement recording. (3) To apply the methodology to specific problems in the perceptual-attentional realm. It is in relation to the last that this technique may offer us a method of attaining an objective indication of what the subject perceives and where and how he directs his attention. With increasing interest in studies involving attention, such a technique would be most useful.

Dr. Carlson has finally made arrangements for obtaining students as a normal control population. Some of these subjects are being tested intensively both as a comparison group for results obtained with patients and as an experimental group for investigating normal relationships among basic psychological processes. An example of the latter is an investigation of the extent to which personality, emotional, and motivational variables are related to the performance aspects of behavior rather than to the perceptual process itself. Another
Section on Perception and Learning (Cont'd)

avenue of inquiry concerns behavioral experimental distinctions between those perceptual processes which may depend more directly upon neural structure independent of experience and those which depend to a greater extent upon development through experience and upon the general psychological state of the individual. These and other researches with this normal population have just recently been initiated, but experience thus far indicates that this program should prove to be a workable and successful operation.

Dr. Blough's studies of techniques for the experimental analysis of instrumental behavior in the pigeon have been further developed and refined. These techniques are proving especially valuable and efficient in the study of the basic processes involved in the stimulus control of behavior and in the study of certain responses which would be difficult to explore with more traditional methods. For example, the pigeon has been successfully trained to stand still for food reward, a response which promises to be particularly useful in assessing effects of the tranquilizing drugs. Chlorpromazine was found to increase the ability of the pigeon to stand still, whereas pentobarbital reduced this ability. In many respects pentobarbital, though not a tranquilizer, has effects which are difficult to distinguish behaviorally from those of the tranquilizing drugs. This emphasis on exploratory work with drugs, however, is now being shifted more toward elucidation of the behavioral principles themselves which underlie stimulus discrimination and stimulus generalization.

Most of the physical construction and equipment procurement for Dr. Calhoun's Rockville Farm Project has been achieved, and initiation of the first pilot studies should be possible by the end of this year. This project will enable more comprehensive controlled study of the environmental and genetic modification of biological systems. Some provocative findings are emerging from present studies in this area. Analysis of two field studies of mice and shrews living in woodlands revealed that the several species forming the community express a social hierarchy in their utilization of space. The more dominant species enjoy greater home ranges, but within each range the individual members of each species maximize distance from other individuals. Behavior of the rat in an activity alley shows a negative exponential relationship between frequency and duration of the behavior, and the frequency with which trips are terminated from a starting point is inversely proportional to distance. It is not known yet to what extent principles describing the utilization of space through time by small mammals will be generalizable to man, but the movement of an animal within its own home range have been found to describe the distribution of church members about a church, and the emotional past history of a rat appears to alter its utilization of space and time. Initial studies have suggested the possibility that emotional conditioning processes may affect space-time utilization through function of the reticular activating system of the brain stem. This and other physiological hypotheses will be further explored in relation to variables of environmental structure and social organization.
SECTION ON ANIMAL BEHAVIOR

In general, this year's activities have concentrated on specifying more precisely the behavioral deficits following brain damage, delineating more exactly the anatomical systems related to cognitive behavior, and developing automatic-testing devices for use in these problems. We have been unable to pursue that part of our program concerning the emotional and motivational aspects of behavior as actively as intended because of lack of funds and personnel.

The study involving the effects of frontal-lobe damage on delayed-response type tests in chimpanzees has been completed except for the last stages of anatomical analysis. The results of this study indicate that chimpanzee performance like that of monkeys is impaired following frontal-lobe damage. Unlike monkeys, however, they are able to recover from these effects and after several months of training regain their preoperative performance level. Thus, at the end-point of their training the effects of frontal-lobe damage in chimpanzees resembles that in man where no consistent effects of frontal-lobe damage on problem-solving behavior have been demonstrated. This study has served a valuable purpose in clearing up some discrepancies in the literature, and in demonstrating the important point that in the highly developed brain, the effect of damage in a particular area may be less than in the more primitive brain.

The work on the effects of brain lesions on social behavior in primates may be summarized as follows: Unlike the findings in monkeys, social dominance in chimpanzees appears to be unaffected by temporal-lobe lesions. Further, frontal lobe lesions in chimpanzees produce a temporary decrease in dominance. This finding is compatible with the subduing effects in the famous chimpanzees, Becky and Lucy, but is in the opposite direction to the effects of such lesions on social behavior in monkeys (i.e., increased dominance) described by Rosvold and Brody. In monkeys our studies show that hippocampal lesions do not affect social dominance; this is an unexpected finding, since lesions in the amygdala, which is anatomically and functionally closely related to the hippocampus, produce striking decreases in dominance. The studies on the interrelation between postoperative experience and brain lesions in determining postoperative change suggest that postoperative experience can determine this effect to some extent; this research area, which is of considerable theoretical importance, unfortunately cannot be pursued at present.

A number of centrally-acting drugs have been investigated with the continuous performance technique: chlorpromazine, L.S.D., meperidine, several barbiturates, meprobamate, benzactyline and d-amphetamine. The results suggest that agents which appear to depress activity in the brain-stem reticular system will impair performance on the C.P.T. These
Section on Animal Behavior (Continued)

Data appear to mesh nicely with the results of our epilepsy studies: those patients in whom the focus of abnormality is presumably in the brain-stem region perform more poorly on this test than other patients in whom the pathology, although equally great, is confined to cortical structures. Other tests of "brain-damage" that have been used have failed to differentiate the cortical from the non-cortical subgroups.

The new, improved version of the C.P.T. has recently been delivered to us and should provide great flexibility in investigating the parameters of the task. In addition, it will make possible precise study of clinical ictal and subclinical ictal phenomena (recorded electrographically as hypersynchrony) in relation to the maintenance of vigilant or attentive behavior. The instrument has aroused interest among other investigators by virtue of its versatility and capacity to elicit and measure behavior that could not be handled so efficiently previously.

The study of the role of inferotemporal neocortex in visually guided behavior is being approached in a variety of ways. Attempts to delineate the anatomical connections between the inferotemporal region and the primary visual system have finally met with at least tentative success. After removing the temporal lobe in one hemisphere and the occipital lobe in the other, monkeys were trained to discriminate visual stimuli. The corpus callosum was then cut in these animals and they were re-trained on the same visual discrimination. Marked impairment in re-learning was found, suggesting callosal transection had interrupted long association tracts, running presumably from the intact occipital lobe through the corpus callosum to the opposite intact temporal lobe. The lack of impairment following various control operations demonstrates that the deficit in the experimental animals was specific to their particular combination of lesions. Final evaluation of these results must await replication of the experiment and histological examination of the lesions. This positive finding is of particular interest in view of the consistently negative findings that have been obtained in animals with subcortical damage. Thus, neither the pulvinar nucleus in the thalamus, nor the superior colliculus appear to serve as an essential relay station between the inferotemporal region and the primary visual system. Now it appears, on the basis of preliminary results from monkeys with combined pulvinar and collicular lesions, that the two structures in combination are not the essential relay stations. At the moment then, cortical-cortical connections appear to be implicated.

The finding that temporal-lobe damage produces visual impairment in monkeys would be of greater theoretical interest if similar results could be obtained in man. Unfortunately, there is little evidence to
support such an extension of the animal data. A reasonable explanation for this discrepancy has been gleaned from recent work on chimpanzees. It was found that bilaterally symmetrical inferotemporal lesions produced impairment of visual discrimination in chimpanzees which had shown no impairment after only a unilateral removal. The negative evidence in human patients may be due simply to the fact that temporal-lobe pathology in man is rarely, if ever, bilateral and symmetrical. Recent work with monkeys, however, has demonstrated that even unilateral damage may produce impairment if vision is limited to the field opposite the lesion. On the basis of these results an experiment has been planned to test for possible differences between tachistoscopic recognition in the left and right visual fields in patients with left or right temporal-lobe pathology.

The evidence which has been accumulated so far supports the notion that the inferotemporal region constitutes one link in the chain of cerebral structures serving vision. The study of the neural activity of this region should provide important information on the sequence of cerebral events intervening between stimulus reception at the cortex and the motor response. Experiments are therefore being planned in which the inferotemporal cortex will be electrically stimulated or recorded from during the learning and performance of visual discriminations. Evidence for disruption in performance following stimulation or changes in electrical activity during learning would bring us one step closer to an understanding of the neural processes underlying vision and perhaps other modalities as well.

An important discovery has been that subcortical structures, such as the head of the caudate nucleus and the splenium of the corpus callosum, are involved in performance on delayed-response-type problems. Several points have been raised by these findings. (1) What anatomical relationships exist to account for these findings? Anatomical studies are under way to answer this question. (2) Are these effects in fact similar to those apparent in animals with frontal lesions? Studies are under way comparing animals with caudate lesions and frontal lesions on a variety of tests. (3) What other subcortical structures may be involved? Studies are under way in which animals are being tested after lesions in other subcortical structures. (4) What functional relationship could exist between the frontal cortex and the head of the caudate nucleus to account for their similar effects? Evoked potential studies are planned to answer this question.
The Laboratory has continued its efforts to understand the nature and the implications of the ion movements fundamental to the initiation and propagation of a nerve impulse and it has made substantial progress.

The squid giant axon, which first allowed the direct measurement of the ionic currents through a nerve membrane, remains the most useful source of experimental information. The continuing improvements of techniques and equipment have resulted in data on this axon that more closely approach the ideals of accuracy, reproducibility and significance than heretofore. The transient and steady state ion current flows after an abrupt change of the potential difference across the membrane are determined much more by the values of the initial and final potentials than by the difference between them. For an initial hyperpolarization depending upon the axon and its condition, these currents approach maxima which are determined only by the final potential and correspond to the rather surprisingly high peak conductances of 200 m mho/cm² for both sodium and potassium.

Further investigation of the effects of external calcium and magnesium ions added further evidence of the qualitative similarity of the actions of these ions. A decrease of either ion concentration tends to increase the membrane excitability by allowing sodium current flow at a reduced depolarization, and in spite of the opposing increase of potassium conductance and more easily evoked sodium inactivation. In procaine the potassium conductance and sodium inactivation changed slightly in the directions instability, but the decrease of sodium conductance and the increase of depolarization required to achieve it accounted for the net stabilizing effect and suggest that procaine not only reduces the number of available paths for sodium ions but also increases the difficulty of opening each path.

Not only do the speeds of the sodium and potassium processes increase by a factor of three for a ten degree centigrade temperature rise as previously reported, but the peak conductances of both of these ions also increase by about sixty percent. In addition to confirming a preliminary report that the squid axon action potential is almost identical in artificial sea waters containing either the normal sodium ion concentration or the same concentration of lithium ion, it was found that none of the ion conductance characteristics are probably changed by more than twenty percent by this substitution. Both the temperature and the lithium effects invite explanation in terms of nonspecific physical processes rather than chemical reactions. A complete analysis of the many records of the ion currents has been delayed by the need for a critical examination of several methods, including those originally used by Hodgkin and Huxley, for the separation and empirical representation of the sodium and potassium components.

An investigation of some characteristics of a lobster giant axon has been completed. The changes of the resting and action potentials produced by alterations of the normally occurring external cations, and by some organic solvents, are compared and contrasted with those found in the squid and other axons in forthcoming reports. The disparities between the activities of synthetic anti-cholinesterases on the enzyme and on frog nerve were
found to include the optical isomers of one compound before the work turned
to the more critical experiments on a single node. Some progress was made
towards the determination of ionic conductances of a single node before the
project was suspended.

Recalculations of the Hodgkin-Huxley equations for the squid axon on an
IBM 704 have shown that mistakes in earlier computations were not of physio-
logical importance although they had been the source of some theoretical
difficulties. The new analog computation program has begun with a systematic
examination of simplified Hodgkin-Huxley equations in which one or more
variables are held constant. One result is that either a constant potassium
conductance or a constant sodium inactivation produces a plateau in the
recovery of the action potential rather similar to that of heart muscle cells.
An investigation of passive iron wire models of nerve activity resulted in
the first quantitative theory of one such system.
LABORATORY OF NEUROANATOMICAL SCIENCES

William F. Windle, Chief

The Laboratory of Neuroanatomical Sciences occupies space in D Wing of the Clinical Center and the East Wing of Building 9. In addition, certain research projects have facilities in Puerto Rico. There have been no changes in the regular professional staff during 1957.

Section on Development and Regeneration

This report of the activities of the Section on Development and Regeneration will be divided for convenience into work in the Bethesda and the Puerto Rican laboratories. Professional personnel at Bethesda are: Lloyd Guth, Richard L. Sidman, Irene Miale, Kenneth M. Wolf and William F. Windle, Chief. Harry H. Wilcox, of the University of Tennessee, is a consultant. Those working in San Juan, P. R., are: C. J. Bailey, J. A. Ranck, S. A. Altmann. Marisa I. R. Ramirez de Arellano and Max Ramirez de Arellano are consultants. C. A. Pfeiffer, J. G. Frontera and W. Stiehl of the University of Puerto Rico Medical School, are collaborators.

Projects at Bethesda:

Histological studies of the spinal cords of cats, paraplegic for 1-2 years, have been continued. Regenerative activities of central nerve fibers which succeeded in traversing the site of the transection under the influence of such agents as piromen were blocked by encroachment of massive scars which apparently were formed from the pia mater, dura mater and surrounding tissues. Vascularity of the site of transection increased with time and the adventitial sheaths of the vessels provided routes for regeneration into both the rostral and caudal portions of the spinal cord by nerve fibers, principally from the spinal nerve roots. Anatomical confirmation of successful regeneration of central fibers of the mammalian spinal cord has been published by scientists in another laboratory and plans are being formulated for collaborative experiments with monkeys in our laboratories late in 1957 or early in 1958.

Dr. Guth has continued investigations of neuron specificities. He has succeeded in restoring motor function to the rat's diaphragm by anastomosing the central end of the cut vagus with the distal end of the cut phrenic nerves, demonstrating that visceral motor fibers can take over the function of somatic motor neurons. Dr. Sidman has carried out experiments by other techniques to explore trophic properties of nerve fibers. In the adult newt, the epidermis plays a special role in limb regeneration but this is not under nervous control. Motor nerve fibers regenerating into the limb do not enter the epidermis.
Studies of development of intrinsic brain structure in the human embryo have been confined principally to assembling and correlating information from the literature. Dr. Guth has translated Ramon y Cajal's classic, but now almost inaccessible monograph, entitled: "Etudes Sur la Neurogenese de Quelques Vertébrés". It is expected that his translation will be published next year.

Studies of the process of aging in the nervous system, have been continued, mainly by Dr. Wilcox, working on contract with the University of Tennessee School of Medicine. In well-controlled material from the brains of guinea pigs between birth and extreme old age, he has found that the process of aging involves a decrease in interneuronal substance (neuropil). During the year a conference on the Process of Aging in the Nervous System was held at Bethesda, the proceedings of which are being edited for publication.

A tissue culture laboratory in Building 9 for Dr. Sidman's use has been under construction for the past year and now is nearly ready for operation. In the meantime, Dr. Sidman has devoted his energies to other types of work, notably, study of the structure and chemistry of photoreceptor cells in several species but especially the squid. Dr. Feder of NIAID, Laboratory of Clinical Investigations has collaborated. Details of their study of fine structure and histochemistry of visual elements are presented in their annual report.

Studies of effects of reserpine and other drugs on monkeys and chimpanzees which produce states resembling parkinsonism in man are being terminated. Results of an attempt to abolish the hypokinesia, rigidity and tremor in monkeys by alcohol injection of the globus pallidus were reported at the First International Neurological Congress in Brussels in July by Drs. Feringa and Windle. The tremor and rigidity was abolished transiently on the contralateral side but returned within 24 hours in chronically reserpinized monkeys. Perhaps the most significant observation resulting from research in this area is that obtained from histological study of the brains of African green monkeys kept on minimal daily doses of reserpine (0.2-0.6 mg/kg) for over 18 months. In contrast with control of material, neurons of various brain stem nuclear groups and cerebral cortex (but not cerebellum) show a high incidence of vacuolation in nucleus as well as cytoplasm. The contents of the vacuoles have not been identified. The significance of the observation is unproved, but it would appear that continuous administration of the drug reserpine, in doses comparable to those in common use in human subjects, may not be without adverse effects on the cytological structure of the primate nervous system.

Other activities of the scientists in the Bethesda component of this section pertain to interpretation of function of neural elements by techniques of histochemistry and fluorescent microscopy. An investigation of the development of the blood-brain barrier has begun (see annual report by Wolf).
Projects at San Juan: During 1957 two groups of laboratories were established at San Juan, Puerto Rico, one adjacent to the Medical School of the University of Puerto Rico and one on the grounds of the U. S. Public Health Service Clinic. Facilities on the small island, known as Cayo Santiago, where a free-ranging colony of about 250 Macaca mulatta monkeys is located, were renovated. A caged colony of 35 breeding females in the San Juan laboratories, and one of about the same size in Bethesda have been established. These several facilities provide for studies of adverse factors in the perinatal period of monkeys which may lead to neurological and psychological deficits in the offspring. Pilot studies have been carried out in guinea pigs and cats.

The principle topic of research at present is asphyxia neonatorum in relation to neurological and psychological deficits in the offspring of monkeys. Before summarizing this work, a number of other topics, touched upon during the year, are noteworthy. (a) Dr. Ranck and others have been standardizing procedures for a neurological examination of the monkey from birth to maturity. This became necessary when it was found that no standard procedure existed. (b) Certain adverse effects of hormonal imbalance during gestation have been investigated in the cat by Dr. Windle. Dr. Pfeiffer is studying endocrine organs of monkeys subjected to various degrees of anoxia or asphyxia. (c) Anthropometric studies are being carried out in the free-ranging monkeys on Cayo Santiago as well as on specimens in caged colonies. This part of the work will soon be taken over by Dr. James A. Gavan of the Medical College of the State of South Carolina on a collaborative basis. (d) An opportunity presented itself to study hemolytic anemia during pregnancy of one monkey in the caged colony. The fetus of this animal was dead at delivery and the mother went into eclampsia with convulsions and urinary shutdown. This appears to be the only reported example of this condition in a primate other than man.

One of the main objectives of the project in Puerto Rico is to relate episodes of asphyxiation at birth to possible deficits in learning ability and behavior patterns after birth. Dr. Bailey has completed a study of learning in guinea pigs 1-2 years old, half of which were asphyxiated and resuscitated at birth. He succeeded in demonstrating that ability to perform in certain mazes was impaired even after the animals had attained adult stages. In this same group of animals Dr. Marisa Ramirez de Arellano carried out studies of the electrical activity of the brain. She established the characteristics of EEG's in the normal animal at different ages and found that abnormalities manifested themselves in some of the asphyxiated guinea pigs. All the guinea pigs of this group have been killed by the perfusion fixation technique and the brains are being prepared for histological study.
A two-year study of behavior and social organization was begun on Cayo Santiago in June 1956 by Stuart A. Altmann (see his annual report). The free ranging colony of monkeys provides a unique opportunity in the new world to make controlled observations, not only of adults but also of newborn and infant monkeys. These observations will help interpret the behavior of controls as well as asphyxiated infant and young monkeys of the caged colonies.

The feasibility of breeding monkeys in caged colonies has been thoroughly established. To date 24 timed pregnancies have been obtained in the caged colonies, which numbered only 24 females at the end of January and has gradually increased to 70.

The main endeavor since establishment of caged colonies of monkeys, beginning the end of January 1957, has been to study acute effects of asphyxia neonatorum induced near the end of gestation in cesarean section delivered animals or within a few days after birth in vaginally delivered animals. This, in a sense, has been an exploratory investigation. To date, the principle results have been as follows: Survival time after asphyxiation appears to vary inversely with age of the subject. At the end of gestation (164-168 days) monkeys were readily resuscitated after 13 or 14 minutes of asphyxiation. By 7 weeks of age the maximum time of survival in an atmosphere of nitrogen was less than 4 minutes. All infant monkeys subjected to experimental asphyxia neonatorum exhibited marked neurological deficits after resuscitation. The acute effects were impairment or cessation of respiratory activities, impairment of the establishment of consciousness, blocking of sensory functions, blocking of reflexes, depression of the rate of the heart beat with abnormalities in the EKG, blocking of visceral functions. Recovery of many of these functions occurred gradually with time. However, all animals remained unnaturally quiet and presented acute nursing and care problems, inasmuch as they lost the ability to suck. By 24 hours after resuscitation, most of them improved to such a degree that the investigators expressed optimism for eventual recovery. However, by 36 to 48 hours, the condition of those which were most severely asphyxiated deteriorated markedly; muscle fasciculation, nasal regurgitation, impaired motor and sensory functions, somnolence, visceral disturbances, status epilepticus, and respiratory arrest were encountered.

Most of these young animals were killed at different ages for histological studies. Some of them are still living and being used for psychological studies together with randomly chosen babies delivered by similar techniques. Sections of the brains of 6 monkeys have been examined. These were animals killed between 2 hours and 6 days after resuscitation. They have been compared with similar sections from control
brains. Extensive cell changes are evident in the brains of all the experimental animals. The only animal which showed petechial cerebral hemorrhages was the one which exhibited status epilepticus. In 5 others the principal abnormality appeared to be neuronal lysis. This was found throughout, but the changes were more marked in the cerebellum, dentate nucleus and certain centers of the brain stem than in the cerebral cortex or basal ganglia. The damage was diffuse rather than focal. It was of such a nature that, had the animals lived for 6 months or more, it might have been difficult to ascertain with certainty that structural abnormalities existed. Such changes after asphyxiation at birth have not been reported in any primate.

Section on Experimental Neuropathology

The professional personnel of the Section on Experimental Neuropathology consists of Helen J. Ramsey and Jan Cammermeyer, Chief.

The main objective of the section has been to reveal factors concerned with development of the myelopathies. Research activities have been directed towards three aims:

1. To develop a procedure which permits an estimation of volume of the spinal cord on the basis of the animal's size and then to conclude whether the spinal cord is affected in a given experimental situation. Another procedure attempts to predict the size which the spinal cord will attain after several months of growth of the animal. Such information is needed for an evaluation of long term experiments. In the course of these studies sex, age and species have been found to be the factors influencing the size of the spinal cord.

2. To study the distribution of extradural fat. This study has been almost completed by Dr. Ramsey in several species of animals of different age. Although certain specific patterns have been established in the distribution of fat, the amount of fat is quite variable. This would seem to be another factor of importance for the proper functioning of the spinal cord.

3. To perfect histological techniques for the purpose of establishing standard conditions of microscopical investigations of experimental myelopathy. After having critically surveyed the technical procedure, the investigators are now in position to evaluate properly subtle changes of neurons, myelin and glia and to dismiss as not significant certain other changes usually encountered in microscopical material, such as variability in the staining of neurons, the size of
glia and appearance of myelin. The emphasis has been placed on formulation of standard procedures for examination of the spinal cord in animals because only when such formulation is completed is one able to correlate moderate functional neurological dysfunctions with subtle morphological changes. This will be necessary before an attack can be directed against the problems concerned with the development of myelopathies.

Section on Functional Neuroanatomy

Professional personnel of the Section on Functional Neuroanatomy are: Leo C. Massopust, Richard Gacek and Grant L. Rasmussen, Chief. This section concerns itself primarily with nervous pathways and connections of the brain and spinal cord.

The origin and termination of the medial longitudinal fasciculus in the brain stem and spinal cord by means of axonal and terminal degeneration methods have been studied by Drs. Massopust and Rasmussen. The termination of spinal components of this tract, consisting chiefly of vestibulospinal fibers, has been more definitely localized to cell groups of the spinal gray matter; in the brain stem the medial longitudinal fasciculus has been found to send some of its fibers beyond the midbrain to the subthalamic region.

Studies on the auditory afferent and efferent systems have been continued by Dr. Rasmussen, with the cochlear nucleus receiving particular attention during the past year. The experimental anatomical findings indicate that the dorsal cochlear nucleus plays an important role in control over cochlear nerve afferents received by the ventral cochlear nucleus. The vast majority of cochlear nerve fibers terminate in the ventral nucleus while the dorsal cochlear nucleus receives predominantly short and long efferent or feed back connections from different parts of the central nervous system.

Mr. Robert Boord, a graduate student of the University of Maryland, worked during the summer on a problem dealing with the innervation of the chinchilla inner ear. This study will be completed at the University of Maryland and NIH during the coming year.

The efficaciousness of the synaptic stain developed by Dr. Rasmussen has been further explored and tested on various synapses in different regions of the central nervous system. It has proven to be specific for demonstration of a "granular synaptic substance" in practically all endings in the young as well as the adult animal. The clarity and completeness of staining is a virtue taken advantage of in present studies of interneuronal relationships by the experimental method of Wallerian degeneration. Disappearance of synapses related to neurons
damaged can be noted and the relative number of synaptic connections playing upon a single nerve cell that originates from different anatomical and functional sources may be determined. In studies of normal material dealing with the maturing terminals of young kittens, this technique shows that synapses make their appearance much earlier than previously noted, a finding which correlates more nearly with behavior studies of the young.

Dr. Chaco of India, guest of this section during one month of the summer, employed the synaptic stain successfully to a problem dealing with synaptic endings of the spinal cord of lower vertebrates.

Section on Neurocytology

The professional personnel of the Section on Neurocytology are:
Milton W. Brightman, R. Wayne Albers and Sanford L. Palay, Chief.
Dr. Samuel McGee-Russell, Birkbeck College, University of London, spent the year with this section as a Visiting Scientist. Dr. Jean Gruner, University of Strasbourq, was a guest in the laboratory for a two-month period, January to March. The principle objective is to conduct research into the fine structure of the nervous system, histochemistry and neuro-secretion.

A laboratory for studying fine structure by means of electron microscopy has been activated during the past year with the installation of an electron microscope and associated equipment. Investigation of the structure of synapses and neuron-glia interrelations in the brains of fish and mammals is in progress. Dr. Palay attended an international symposium on the structure and function of the neuron held in Caracas, Venezuela, at which he presented a paper on the ultrastructure of the synaptic junction.

Drs. Brightman and Albers have studied the distribution of true and pseudocholinesterase activity in the central nervous systems of cats and rats. The perikarya of neurosecretory neurons contain true cholinesterase activity whereas their endings in the neurohypophysis do not. Pseudocholinesterase activity occurs in the glial cells of the cat's spinal cord whereas in spinal cord and brain of the rat, activity is confined to the vascular endothelium. This observation may be related to the locus of the blood-brain barrier and may be helpful in an analysis of myelogenesis.

Drs. Albers and Brightman have also completed an interesting study of dilute alcohol extracts obtained from frozen sections of the neurohypophysis of the rat. These extracts contain a proteinaceous material which is present in large amounts in the neurohypophysis of
hydrated rats but is absent from the glands of animals given restricted amounts of water for several days. When this material was assayed, the investigators found that practically all of the antidiuretic hormonal activity of the neurohypophysis was in this fraction. Since it has been known for several years that the neurohypophysial hormonal activities can be isolated in small molecules (octapeptides), this work demonstrates that the active natural hormones are not secreted as small molecules but are in fact associated with a protein.

Dr. Albers, in association with Dr. Brady of the Laboratory of Neurochemistry, has been studying the localization of glutamic decarboxylase in the nervous system. This enzyme is absent from white matter, the neurohypophysis and the pineal gland, but is high in certain areas of the gray matter. The reaction which this enzyme catalyzes results in the production of γ-amino butyric acid, which is an inhibitor of synaptic transmission. The localization of this enzyme is therefore of undoubted importance in an analysis of cerebral metabolism and function.
During the past year, efforts to recruit a chief for this laboratory were continued. We identified successively two distinguished investigators each of whom could mount a most impressive and fruitful program of research in this field. Each was greatly attracted to the Basic Research Program. The only handicap was lack of sufficient space. Each was willing to give up much of the luxury of space where they were in favor of the values of interdisciplinary transaction available here. But if they came here they would have to amputate too much of what they want to do and are prepared to do, in order to be accommodated within the space we have available. We considered a number of alternate plans for re-arrangement of space available to the Basic Research Program as a whole, in order to make this key recruitment possible. We tried to win back space which historically had been "loaned" outside the Basic Research Program. In every case, we failed. Each of the scientists concerned would have been content to join the Program, do as much as possible with the space presently available and await the construction of new space, provided only that we could indicate that such construction would probably take place within a few years. There are clearly many uncertainties in such contingency. Therefore, the matter was dropped for the time being. Until more space becomes available, it will not be possible to establish the one or two additional Sections and bring to the Laboratory the overall leadership needed to fulfill our research objectives in Neurochemistry.

Meanwhile, the two already established Sections have continued to demonstrate that they are capable of pursuing important issues profitably. The Section on Physical Chemistry under the leadership of Dr. Alexander Rich, has made significant advances in the determination of the shape and dimensions of several families of large molecules. These are variously concerned with cell replication and growth, the "coding" of amino acids along protein strands, the control of protein conjugating systems by metallic ions, the binding of key metallic ions to protein complexes, and the structural role of certain protein-steroid complexes relating to myelin. The Section has already received wide recognition for its investigations concerning the structure of collagen, DNA and RNA and for its comparative studies of natural and synthetic polynucleotides. The key to many problems
of importance to an understanding of the nervous system will be found by examining the shape and activity-configuration of these molecules.

The Section on Lipid Chemistry, led by Dr. Roscoe Brady, has completed a year of accomplishment in relation to our understanding of lipid formation and structure, and of the mechanisms of action of certain nimble elements concerned with the initiation and inhibition of the nerve action potential. Sphingosine synthesis has now been accounted for, the mechanism of incorporation of glucose and galactose into cerebrosides has been shown and a further advance has been made toward defining the nature, origin and disposition of myelin. Gamma-amine butyric acid has recently caused quite a stir among neurophysiologists and neurochemists as an example of a synaptic inhibitor comparable to the synaptic excitants such as epinephrine and nor-epinepyrine. The Section has contributed toward knowledge of both the source and fate of this compound within the brain. By combining talents with the Section on Special Senses in the Laboratory of Neurophysiology, Dr. Brady has found that compounds releasing free radicals, and compounds interfering with certain redox potential mechanisms within the squid axon may provide an avenue of approach for the ultimate chemical analysis of the mechanisms governing the nerve action potential.

Summary reports prepared by the Section Chiefs follow:
Section on Physical Chemistry
A. Rich, Chief

One of the main activities of the Physical Chemistry Section consists of studying the properties and physical structure of ribonucleic acid. This substance, an elongated polymeric molecule composed of a sequence of nucleotide units, has been shown to be of fundamental importance in the economy of the cell. It is found in the microsomal particles which are the site of protein synthesis. It is believed that the RNA in these particles somehow determines the sequence of amino acids in the protein to be synthesized. Thus, the RNA has an important function in transmitting information, i.e., concerning amino acid sequences, from one polymeric species (nucleic acids) to another (proteins). In addition to this, another function of prime importance is the transmission of genetic information. Thus, it has been shown that RNA can act as a carrier of genetic material in several RNA-containing viruses. In this role, the RNA acts as a carrier of information from one nucleic acid molecule to a large number of nucleic acid molecules in the daughter viruses. In this respect, RNA shares this ability with deoxyribosenucleic acid (DNA) which is the main carrier of genetic information.

In view of the participation of RNA in these two fundamental cellular processes, the Section on Physical Chemistry is studying the molecular architecture of the RNA molecule in the hope of elucidating its molecular structure in order to obtain an understanding of the molecular mechanisms behind these activities. In this regard, it is quite possible that the role of this molecule is even more significant in nervous tissue than in other tissues since an essential activity associated with nervous tissue is information transfer. How this is accomplished on the molecular level in nervous tissue is of course unknown at the present time. However, fragmentary information is available which suggests that the nucleic acids play an essential role in this activity.

The Section on Physical Chemistry has been studying the synthetic polynucleotides. These are molecules composed of the same linear array of nucleotide subunits as is found in the naturally occurring nucleic acids. However, they can be prepared enzymatically and, what is most significant, the sequence of nucleotide bases can be controlled during the polymerization. Thus, it is possible to prepare not only a nucleic acid-like molecule which has all four of the constituent nucleotides found in naturally occurring RNA, but it is also possible to prepare nucleotide polymers which contain only one nucleotide. This is of fundamental importance in terms of elucidating the structure of the molecule since it superimposes a degree of simplicity on the molecule which is not found in nature. This simplicity permits us to study the configurational details of the molecule in a form which is simplified to a point where we can solve the problem.
About a year and a half ago, we discovered that two of the synthetic polyribonucleotides, polyadenylic acid and polyuridylic acid, would combine together to form a two-stranded helix in which the uracil and adenine residues are hydrogen bonded to each other with a specific set of hydrogen bonds. These are, in fact, the same type of hydrogen bonds which hold together the two-stranded helical DNA molecule. This discovery attracted a great deal of interest because it showed how intimate was the relationship between DNA and RNA. As was noted above, both of these molecules have the ability to transmit genetic information, and this discovery has led to the tentative conclusion that both molecules carry out this function, using the same molecular mechanism, i.e. separation into two single strands with the formation of a complementary strand to yield two identical molecules.

During the last year, we made a series of additional discoveries. Among the first of these was the discovery that it is possible to make a three-stranded nucleic acid. Thus, when the two-stranded polyadenylic acid plus polyuridylic acid is put into a solution with an additional molecule of polyuridylic acid and small amounts of magnesium ions, it will combine to form a three-stranded molecule. This three-stranded molecule was discovered by a spectrophotometric and ultracentrifuge investigation. More recently, a detailed X-ray diffraction pattern has been obtained from which we will be able to work out the details of the molecular arrangement of the three chains. This is the first time that a three-stranded nucleic acid molecule was discovered, and it may be significant in pointing out the manner in which nucleic acid molecules function. One of the probable reactions of the DNA molecule is that it aids in the specific synthesis of an RNA molecule. By doing this, it transfers information, i.e., nucleotide sequence from one polymeric species to another. It is possible that this is accomplished by forming a single-stranded RNA molecule which is wrapped around a two-stranded DNA molecule. Accordingly, the discovery of three-stranded nucleic acids seems of potential importance.

Further investigations concerning other polynucleotide interactions have been carried out, and several have been discovered. Among the first of these was a combination involving polyadenylic acid with polyinosinic acid. Polyinosinic acid is closely related to polyguanylic acid and as such is of importance in our understanding of the naturally occurring nucleic acids. It was found that polyadenylic acid and polyinosinic acid would combine together to form a two-stranded helical molecule. It was also found that an additional strand of polyinosinic acid could join the two-stranded complex to form a three-stranded complex, polyadenylic acid plus 2 polyinosinic acid. This is, of course, similar to the system polyadenylic acid plus 2 polyuridylic acid.
Another discovery was made concerning the interaction of polyinosinic acid and polycytidylic acid. These two molecules will combine to form a two-stranded helical arrangement. It is interesting to note that this two-stranded molecule will not form a three-stranded one in contrast to the two systems mentioned above. The most interesting feature of this combination is that it has an X-ray diffraction pattern which is very similar to that which is found in naturally occurring RNA. Accordingly, by working out its structure, we should learn something about the configuration of RNA when it is extracted from cells.

Another discovery was made concerning the structure of polyinosinic acid itself. It has been found that this molecule exists as a three-stranded helical structure with a cyclic system of hydrogen bonds holding together the three strands. Although this structure is quite interesting, it is difficult to relate it to the configuration of the naturally occurring nucleic acids.

If we assess the total amount of information known about the configuration of the synthetic polyribonucleotides, we find that we have deduced a total of eight different structures which will form from these polynucleotides. These provide an adequate basic set of information from which we hope to go on to deduce the configuration of RNA in cellular systems.

While studying the synthetic polyribonucleotides, we have not neglected to study naturally occurring RNA itself. Thus, a study was carried out of methods of extracting RNA from muscle tissue in order to obtain it in an undegraded form. In addition, studies were made of the effects of metal ions on the stability and sedimentation properties of naturally occurring RNA. These have shown that metal ions in small quantities are able to stabilize naturally occurring RNA probably by serving as sites which bind together the negatively charged phosphate groups and thereby decrease the amount of internal electrostatic repulsion energy in these molecules.

Another aspect of the program of the physical chemistry section has been the study of the structure of protein molecules. As in previous years, we have continued to work on the structure of collagen, the major fibrous protein in the animal kingdom. Refinements have been carried out on the molecular structure proposal made two years ago. This proposal has now been accepted quite generally by the scientific community as providing a basis for the structure of collagen. Studies have been made concerning the interaction of different collagen chains with each other and the effect of various amino acids side chains on the stability of the molecule. A recent addition has been the study of elastin, a closely related protein
which provides the elastin components of blood vessels and connective tissues. Preliminary studies of this molecule indicate that it has a structure similar to a somewhat degraded collagen molecule.

An investigation has been carried out on the coordination of the porphyrin group to the protein part of cytochrome C. This has been done by making a thermodynamic study of the binding of various small molecules such as azide or cyanide to the iron atom in cytochrome C. From this, information may be obtained concerning the amino acid side chains which are of importance in holding the heme group to the protein.

Further work has been carried out on the interesting interaction between steroid molecules and amino acids or peptides. These interact to form a helical structure with a diameter of 40 Å. Studies have been carried out on the number of amino acids which will interact with the steroid (sodium desoxycholate). It has been found that a large variety of amino acids and peptides will interact. All of these form the same helical structure although there is some modification of the helix as a function of different amino acids. Further studies are being carried out on this complex to ascertain the molecular configuration of the steroid molecule. Steroids play an important part in the structure of the myelin and fatty components of nervous tissues and it is hoped that these studies will provide some understanding of the modes of packing steroid molecules together. This may lead to an understanding of the unique role which steroids play in the nervous system.
The primary goal of this section is to elucidate the pathway of synthesis and metabolic fate of the complex lipids of the nervous system. This problem has been approached by investigating the formation of several of these components using enzyme systems obtained from brain tissue. The distinguishing characteristic of the major portion of neural lipids is the presence of the long chain dihydroxyamine, sphingosine, which forms the basic structural unit of these complex lipids. Accordingly, an elaboration of the enzymatic mechanism of sphingosine synthesis is of paramount importance for understanding the formation of these lipids. We have succeeded in demonstrating for the first time the enzymatic synthesis of sphingosine (NINDB-NCl) and have characterized the enzyme system and identified the cofactors required for this process. That the reaction is exceedingly complicated is indicated by the observation that at least eleven non-enzymatic components are required for the final step in this process. These findings are of considerable interest since a relative insufficiency of any one of these materials could potentially interfere with the formation of myelin. Furthermore, in the course of these investigations, the pathway of formation of long chain fatty aldehydes has been discovered. These latter materials constitute the characteristic moieties of another group of cerebral lipids called plasmalogens.

Perhaps the most representative of the complex cerebral lipids are cerebrosides. These compounds are composed of an extra-ordinarily long chain fatty acid in an amide linkage with the amino group of sphingosine. A third portion of these compounds is a molecule of either glucose or galactose joined with the primary alcoholic group of sphingosine by a glycosidic bond. We have succeeded in demonstrating for the first time the enzymatic incorporation of glucose or galactose into cerebrosides (NINDB-NC4). The enzyme system obtained from brain tissue has been characterized and the specific uridine nucleotide cofactors required for this synthesis have been identified. Of particular interest was the identification of the pathway of incorporation of galactose into cerebrosides. The experiments performed in this series of investigations indicated that in contrast with the mechanism of formation of uridine diphosphate glucose from glucose-1-phosphate and uridine triphosphate, an analogous enzyme for the formation of uridine diphosphate galactose was absent in brain tissue. The formation of the appropriate galactose nucleotide from galactose-1-phosphate occurred only in the presence of catalytic amounts of uridine diphosphate glucose which indicates the presence of a novel transferring enzyme in brain tissue called galactose-1-phosphate uridyl transferase. It should be indicated here that when glucose is employed as substrate, it is actually incorporated into cerebrosides as galactose confirming the presence of the enzyme uridine diphosphate galactose epimerase in these preparations.
In addition to the fact that cerebrosides are important constituents of the myelin sheath, there are several disease states associated with an overabundance of such compounds, particularly Gaucher's disease or Tay-Sachs' disease. In the latter condition related materials called gangliosides accumulate in pathologic quantities in the brain. We are at present investigating the metabolism of cerebrosides using tritiated galactocerebrosides in these studies. Furthermore, we are exploring the effect of certain antimetabolites such as deoxyglucose and deoxygalactose on cerebroside formation.

Since cerebrosides contain long chain fatty acids as well as sphingosine and a sugar molecule, we wish to investigate the incorporation of fatty acids into ceramides (sphingosine-fatty acid) or cerebrosides (NINDB-NC5). A search for the appropriate tissue source and enzyme system will be initiated shortly.

Another important class of cerebral lipids under investigation in this laboratory consists of inositol lipids. These materials are particularly interesting because they have been found to exhibit the highest rate of metabolic turnover of all of the cerebral lipids. We have demonstrated for the first time the enzymatic incorporation of inositol into this type of lipid and have identified the particular cytidine nucleotide cofactor required for this process (NINDB-NC7). This process was investigated with the use of tritiated inositol and in the course of these investigations several new techniques for the handling and radioactive assay of tritiated compounds have been developed (NINDB-NC8). Of particular interest in this regard was the innovation of the use of silica counting vials which improved the low level counting of tritiated samples immensely. Another technique developed here was the extraction of lyophylized tissue samples with an appropriate solvent system for direct radio-assays of tissue specimens. These techniques proved to be particularly feasible for the study of metabolism of meprobamate, a tranquilizing agent currently in wide use (NINDB-NC9).

The availability of liquid scintillation counting techniques suggested a method which has been successfully employed for the ultra-micro determination of the enzyme glutamic decarboxylase (NINDB-NC2). This enzyme catalyzes the formation of \( \gamma \)-amino butyric acid, a compound found to exert striking neurophysiological effects. We have succeeded in identifying three particular regions where this enzyme is predominantly found in the central nervous system. These areas comprise the reticular formation of the midbrain, the optic sensory area of the cortex, and the nucleus proprius of the dorsal horn of the spinal cord. Such a distribution where a localized production of \( \gamma \)-amino butyric acid can occur may be of considerable significance for mediating certain control mechanisms characteristically exhibited by nuclei such as are found in the reticular formation. This project is continuing by investigating the metabolic fate of \( \gamma \)-amino butyric acid produced by the decarboxylase reaction. It undergoes transamination to form succinic semialdehyde which is subsequently oxidized. The enzymes catalyzing these reactions have been demonstrated and an assessment of the quantitative importance of this alternate pathway of cerebral metabolism will be undertaken.
The investigations of neurohumoral agents led us to the observation that under certain conditions, compounds such as serotonin which contain an aromatic benzene ring are not necessarily formed via the 7-carbon sedoheptulose-diphosphate pathway. Accordingly, we wish to try to identify alternate enzymatic routes for aromatic ring formation (NINDB-NC6). These experiments are pertinent because of the finding that compounds such as benzoquinone capable of giving rise to free radicals have a profound effect on the conduction of nerve impulses. This observation was made in the course of experiments on the intra-axonal injection of enzymes and other biologically active materials (NINDB-NC3). These investigations also revealed that the application of compounds having sufficiently high oxidation potential cause drastic changes in the conduction properties of the squid giant axon. The results seem to indicate that the axon membrane is normally in a reduced state, a condition known to require energy obtained through metabolic reactions, and that the appropriate alteration of this condition permits the investigator to predetermine any number of repetitive responses to a single stimulus that is desired. It appears that a delicately balanced equilibrium is obtained between the oxidizing agent and the reduced axon membrane which can be destroyed by the agent or by allowing the nerve to fire repetitively until it has exhausted its metabolic energy source. Some striking recent observations have been obtained in this laboratory with regard to the ability of brain extracts to reduce exogenous triphosphopyridine nucleotide in the absence of added substrate. Taken together, these investigations suggest certain experiments which should be undertaken which may help to clarify the mechanism of production of the resting potential of a nerve fiber and ultimately, the nature of the metabolic processes responsible for the phenomenon of excitability.
I. ADMINISTRATIVE

Throughout the year the administrative unit of the Addiction Research Center (ARC) continued to conserve the time of the professional staff by efficient handling of purchasing, filing, personnel record keeping, etc. The typing of manuscripts has constituted an especially heavy load during the current year and the editing and bibliographic checking by the administrative staff contributed greatly to smooth preparation of manuscripts and reports. As experience was gained, property accounting, now delegated to the ARC instead of the hospital, proceeded satisfactorily.

The additional subprofessional employees who came on duty during last fiscal year or in the first part of the current fiscal year are now well trained and oriented in their jobs. We were disappointed that request for special awards to the psychiatric aides was not granted. We intend to write another recommendation for a special award for this group in the very near future.

We have experienced difficulty in obtaining professional personnel but have succeeded in recruiting a neuropharmacologist, Dr. William R. Martin, who will come on duty on 1 December 1957. Dr. Martin will initiate a program of studies of the effects of acute and chronic intoxication with various drugs on the activities of single neurons. Studies of this nature are basic to complete understanding of the addiction process.

Space of the ARC has now become inadequate. The animal house, which is a temporary structure, is very crowded and can barely house all of the animals needed. It does not have floor drains, is not sanitary, and should be replaced as soon as possible. The addition of a neuropharmacologist means that crowding in the animal building will be further intensified. It is hoped that the hospital will make an additional ward available to us. This would permit us to convert one of the present wards to additional office and laboratory space.

II. ADDICTIVE PROPERTIES OF NEW ANALGESICS

This is a technological project which is carried on for the protection of the public. As new analgesic drugs are developed that are likely to come into clinical use they are referred to the ARC by the Committee on Drug Addiction and Narcotics of the National Research Council. After the addictive potentialities of these.
drugs have been determined, by methods previously described, the findings are referred to the Committee on Drug Addiction and Narcotics, NRC, who in turn informs the Section on Addiction-Producing Drugs, World Health Organization. These bodies advise the United States Government and the United Nations concerning appropriate legal action regarding control of these drugs at national and international levels.

It is now hoped that in the future most drugs can be tested in animals. Currently, initial tests of addictive properties of new agents are carried out by the Department of Pharmacology, University of Michigan, using monkeys. All drugs are referred to this unit prior to being tested by the ARC. It seems very likely, however, that at sometime in the future some unit of the government (Public Health Service or Food and Drug Administration) may have to take over this animal-testing program.

During the year five new analgesics were tested. Three of these had sufficient addiction liability to justify placing them under the controls of the Harrison Narcotic Act. D-propoxyphene, though possessing some addiction liability, was judged not to be sufficiently dangerous to require control by the narcotic law. No decision has been made in the case of the fifth.

The demethylated congener of morphine (normorphine) was especially interesting. This drug, which is one of the metabolic products of morphine in the body, has been presumed to be relatively inert on the basis of animal tests. Axelrod and his collaborators at the NIMH have shown that ability of the liver to demethylate morphine declines during experimental addiction in male rats. Axelrod felt that this change might be a model of effects on receptors within the central nervous system and might lead to a theory of tolerance. For this reason, normorphine was reinvestigated at the ARC.

In single dose, normorphine is less potent than is morphine in inducing behavioral changes in man. In repeated dose, however, normorphine has accumulative effects and is more potent than morphine. For this reason, the dose cannot be elevated as rapidly as the dose of morphine. Tolerance to the sedative effects of normorphine appear to develop more slowly than does tolerance to the sedative effects of morphine. Normorphine completely suppressed symptoms of abstinence from morphine. Following withdrawal of normorphine after direct addiction (or after substitution for morphine), abstinence appeared slowly and was quite mild as compared with abstinence from morphine.

Although normorphine has definite addictive properties, its addiction liability is the least of any potent drug in the morphine
series. If normorphine is a good analgesic, it will represent a considerable advance toward the goal of a nonaddicting analgesic.

During the coming year this project will be continued, as it must be, in order to protect the public. Primary emphasis will be placed on demethylated derivatives of morphine and meperidine.

III. CHRONIC BARBITURATE AND ALCOHOLIC INTOXICATIONS

A. Substitution of Alcohol for Barbiturates. The project on equivalence of chronic alcoholic and barbiturate intoxications was completed during the year. Alcohol was substituted for barbiturates in a sufficient number of chronically intoxicated dogs to warrant the following statements: in sufficient dose, alcohol reduces the number of seizures after withdrawal of barbiturates, but does not eliminate them entirely. Alcohol suppresses the barbiturate withdrawal delirium completely. Following withdrawal of alcohol after substitution for barbiturates, convulsions were observed in occasional dogs and delirium in the majority of the animals. These findings indicate that chronic intoxication with alcohol and barbiturates are partially but not totally equivalent.

B. Substitution of Chlorpromazine for Barbiturates. Chlorpromazine did not suppress abstinence from barbiturates in dogs.

C. Meprobamate. Special studies were carried out on chronic meprobamate intoxication. Patients who entered the hospital with histories of taking large amounts of meprobamate were maintained on their accustomed dose of meprobamate while opiates were withdrawn. After allowing a week for recovery from abstinence from opiates meprobamate was abruptly withdrawn. A convolution occurred in one of 3 patients and an abnormal EEG was observed in another patient.

Five dogs were chronically intoxicated with meprobamate. The dose was increased as tolerance permitted to 5-6 grams daily, divided into two or three doses. One of the dogs died during the period of chronic intoxication. Following abrupt withdrawal of meprobamate all 4 surviving dogs had severe abstinence. All 4 had seizures and bizarre behavior, and 3 of the 4 dogs died after repeated seizures ("status epilepticus"). These findings show that meprobamate can cause a type of addiction similar to that caused by barbiturates or alcohol.
During the coming year we hope to test the equivalence of intoxication with paraldehyde, chloral, meprobamate, doriden and barbiturates.

IV. BIOCHEMISTRY OF ADDICTION

The biochemical unit shifted from clinical biochemistry into the field of drug metabolism during the year. Methodological problems in this area are particularly difficult because of the relatively low doses of analgesic drugs given human subjects, and because of the high incidence of interference by the various foodstuff and other drugs often ingested by the subjects. A great deal of progress was made in developing paper chromatographic methods for isolation of drugs from body fluids. Methods for quantitative determination of morphine and normorphine were developed. The normorphine method has been particularly troublesome since the solubility of normorphine in organic solvents is less than the solubility of morphine. Quinine appeared to have no effect on the conjugation of morphine. Less normorphine is conjugated than is the case with morphine. This last finding may explain the difference in the length of action and addictiveness of morphine and normorphine.

Addiction to and withdrawal from analgesics and barbiturates had no significant effect on the excretion of 5-hydroxyindoleacetic acid.

During the coming year we hope to complete a project on comparison of the metabolism of morphine and normorphine, and to determine the changes in excretion of epinephrine and norepinephrine during cycles of addiction. We also hope that another chemist can be obtained to initiate a study on the effects of addiction on enzymological processes at the cellular level.

V. NEUROPHYSIOLOGY AND NEUROPHARMACOLOGY OF ADDICTION

Studies on changes in electroconvulsive thresholds during addiction to and withdrawal from barbiturates in cats were hampered by a number of technical difficulties. Although seizure thresholds are elevated and variable during addiction to barbiturates, elevations were also noted in control cats that were receiving no barbiturates. Apparently, repeated electrostimulation causes some change (perhaps anatomical) leading to elevation in the seizure threshold. No consistent change was seen in seizure threshold after withdrawal of barbiturates. Cats addicted to barbiturates had fewer spontaneous seizures if
stimulated on a regular schedule after withdrawal of the barbiturates.

Following withdrawal of barbiturates after chronic administration, one spinal dog had grand mal seizures above the level of the transection but no seizures below. This finding indicates that the barbiturate abstinence syndrome is mediated at levels above the spinal cord.

During the coming year we hope to continue the project on seizure thresholds during addiction to barbiturates, using electroencephalographic changes instead of clinical seizures as the end point. We also hope to begin experiments with animals with chronically implanted electrodes, in the hope of obtaining information on changes at various levels of the nervous system during morphine and barbiturate addictions. It may be possible to begin studies on the relationship of systems subserving synthesis and destruction of acetylcholine in relation to addiction to barbiturates. It is also hoped that studies on the effects of acute and chronic intoxication with various drugs on the activities of single neurons can be initiated by Dr. Martin.

VI. PSYCHOLOGY OF ADDICTION

Physician addicts show less elevation on the Pd (psychopathic deviate) scale of the MMP 1 than do either nonphysician White or Negro addicts. Physician addicts are higher than normal on the neurotic scales. Unfortunately MMP 1 profiles on non-addict physicians are not available and must be obtained before this study can be interpreted properly. We hope to obtain control profiles on a sample of Army physicians.

A great deal of progress was made in the construction of psychological tests for differentiating between the subjective effects of various classes of drugs. Questions which differentiate between the effects of a marihuana-like drug, LSD, morphine, pentobarbital, and amphetamine have been assembled. A general inventory is to be constructed from these items and tested more thoroughly during the coming year on a number of classes of drugs. It is hoped that these inventories will provide quantitative indices of the effects of the drugs which addicts regard as pleasant ("euphoria") so that a more exact statement on relative addicive-ness of different agents can be made.

Studies on the effects of drugs on conditioned inhibition of a feeding response in rats (pain-anxiety) were continued. It was found that different types of drugs produce specific patterns of
unconditioned bar-pressing, time-action rates, and conditioned inhibition of feeding responses. It was also found that very exact control of the strength of the auditory stimulus used is essential to this particular method. The studies indicate that morphine abolishes anxiety in anticipation of a painful stimulus.

A number of studies on the effects of drugs on "mental set" were completed. In this work visual-hand reaction time is determined under two conditions: (1) when various foreperiods (warning periods) are administered in a regular order, and (2) when foreperiods are administered in an irregular fashion. It is known that in "normal" subjects curves obtained with the regular and irregular procedures are well separated. In schizophrenic subjects, the curves cross, indicating a disturbance in ability to profit from the regularization of the foreperiods. This test was administered in random balanced order to 10 former addicts who received morphine, pentobarbital, LSD, placebo, and amphetamine. Amphetamine and placebo had little effect on reaction time or on mental set; morphine and pentobarbital slowed reaction time but did not impair mental set; LSD slowed reaction time, but did not cause any statistically significant impairment of mental set (crossing of regular and irregular curves) in spite of the presence of marked perceptual distortion, hallucination, and depersonalization. These findings indicate that LSD is possible only indirectly related to the natural psychosis, schizophrenia.

During the coming year we hope to complete the study on physician addicts, to develop the inventory for measuring subjective effects of drugs further, to investigate the significance of drug-produced internal changes in controlling animal behavior, and to begin studies of the effects of drugs and addictions on discrimination.
The productivity of the Laboratory of Neurophysiology continues at a high level and is in the van of some crucial arguments. One of the most important current questions is the participation of soma and dendritic membrane in activation of the efferent axons. Nearly 20 years ago it was recognized that sufficient depolarization of the dendrites, or other components, of a neuron could cause the cell body to discharge without actual complete depolarization of said component structures. It was further recognized that sustained depolarization of these structures might result in repetitive firing of the cell body and axon. However, physiology of the neural network has been slow to sufficiently divorce itself from axonology. This is to say that the compulsion to fit CNS ganglion physiology into "the existing framework of knowledge" (which was largely axonology) has acted as a conservative brake on advancement. During the past several years great progress has been made toward liberating thinking from the simple axonology concepts. This has been particularly true of the dendritic components of the neuron. During the past 2 or 3 years it has been quite vociferously argued that the dendritic membrane is entirely passive. It has further been argued that all synaptically covered parts of the neuron membrane are passive and electrically inexcitable (that is they are somehow not capable of complete all-or-none regeneratively propagated discharges) and that the polarization modulation of these parts of the neuron is entirely accomplished by neurochemical means. Whether or not the latter point is correct is not completely proven. But the best evidence so far obtained for the passive nature of the soma-dendritic membrane has been developed during this year by Dr. W. H. Freygang working on the lateral geniculate nucleus of the cat. Using very small pipette electrodes, excellent electrical technics, and superb mathematical analysis, he has developed strong evidence that only a very small area of the neuron soma is electrically excitable. All other parts of the neuron react passively, acting as sinks of current which causes activation of the low threshold axon hillock region. This experiment depends on placing the microelectrode very close to the active membrane so that it measures the IR drop due to the total membrane current at that locus. The only discernible reservation about this experiment devolves on the inevitable Heisenberg uncertainty principle. Has the electrode, because it is so near the membrane, rendered that locus inexcitable? There are many reasons to discard this objection. This experiment is the best and probably the only valid evidence for the electrical inexcitability of the soma-dendritic membrane in the mammalian CNS. So far as it is
possible to accurately judge current events this paper constitutes a revolution and a major breakthrough.

Tests of this theory on the motor neuron (anterior horn cell) done in collaboration with Dr. Karl Frank have more clearly substantiated it. Very recently a concentric pair of electrodes have been used to record simultaneously from inside and just outside the anterior horn cell. This has likewise confirmed Dr. Freygang's observations on the lateral geniculate.

Drs. Tasaki and Spyropoulos, in the section on Special Senses, have made an important advance in axonology. They have found that when the squid nerve is clamped, i.e. an attempt is made to fix an imposed potential difference across the membrane; that the membrane does not respond uniformly but that erratic patches contribute the current and that these patches have the characteristics of local all-or-none reactions. This fact indicates that the normal membrane as a whole is not clamped but that only the electrodes are clamped. This demands re-evaluation of the basic Na-K exchange theory because obviously the current measured and the apparent resistance change are not properties of the total membrane undergoing a smooth continuous function, but are instead the more or less chance resultant of reactions in random patches on the membrane. This change in current flow and pattern of same as a function of the imposed voltage is now regarded primarily as an increase in total area of active patches. Again the inevitable Heisenberg uncertainty principle must be considered. Has the placement of electrodes inside the squid nerve and other items such as dissection of the nerve produced significant local changes in patches of membrane? However, Dr. Tasaki has acquired considerable collaborative evidence in recent years from the single node of toad A fibers and his two stable state experiments. All these items suggest that the normal axon membrane does not exhibit partial states in its reactions except transiently. In the case of the squid nerve under voltage clamp the membrane resistance changes only under the active patches and this current has heretofore been considered to be uniformly conduced by the entire membrane. If the sodium current is not a uniform function of membrane voltage, for instance, the Hodgkin-Huxley theory must be modified.

Drs. Spyropoulos and Tasaki are investigating active chemical processes to account for the action potential. They have used the methods of intracellular injection into the squid nerve and also the single node preparation. In their hands these methods are exquisitely sensitive tools for study of many biochemical problems. Their thesis is that the action potential as well as the recovery process probably involves biochemical events and that the ion exchange is not merely a passive result of a regeneratively propagated action current.
They have made very substantial progress in this direction and we can look forward to decisive and comprehensive conclusions during the coming year.

Drs. Tasaki and Spyropoulos have also determined that the Bekesy potential is generated in the stria vascularis and not by the brain cells of the ear. This confirms or perhaps, is concurrent with similar studies done at Institute for the Deaf at St. Louis, Mo. The source is not in the hair cells.

Recently Drs. Tasaki and Chang have gone to Dr. Pomerat's famous tissue culture laboratory at Galveston. They are making an intensive investigation of electrical reactions in cultured CNS cells.

The program of the laboratory has been considerably broadened and strengthened by the recruitment of Dr. Paul MacLean (Section on Limbic Integration and Behavior). His broad general knowledge in several fields and his work on the limbic system well fills a gap in the program. Dr. MacLean is setting up his laboratory and has already underway a valuable project concerned with use of genetically and chemically induced sub-cortical lesions in rats.

The Section on Cortical Integration has continued work on the remarkably successful chronic monkey technic. Stop stimulus and start stimulus regions have been partially mapped and work on this aspect is continuing. Regions concerned with pleasurable and compulsive activity are being clarified as well as regions concerned with negative emotions and pain, anxiety, and fright. The importance of such work for problems of mental health needs no elaboration.

A new technic for implanting of electrodes has been developed and successfully used on the monkey and the porpoise. The latter animal (2 preparations) has shown learning processes faster than the monkey by an order of magnitude. Considering the fact that the porpoise possesses one of the most elaborately developed of the mammalian brains, this fact constitutes a very interesting observation.

Work is continuing on a practical method of portraying and analyzing activity from 256 electrodes. The section enjoyed the opportunity of collaborating with Dr. H. Magoun for a few months.

It is gratifying to note that Dr. Lilly is one who is actively engaged in chronic electrode work in primates and that he is deeply conscious of medical and social responsibility involved. He is not encouraging brash clinical work and is attempting to do constructive work to encourage only conservative, well considered activity in that direction.
The Section on the Spinal Cord has continued with elegant work. It is to be remembered that this laboratory by virtue of its technical excellence was the first to demonstrate that an accurate intracellular record of antidromic activation showed two components. Dr. Frank's consultation and collaboration with Dr. Freygang has been particularly valuable and gratifying. This has led to important comparisons of records taken from within the cell and just external to it by means of a double concentric electrode system.

They have discovered a "remote" inhibition process which operates without any detectable change in the polarization of the cell membrane as measured by intracellular electrodes. This laboratory is "tooling up" for transmission of neurochemical agents through their pipettes.

Work has been continued on spreading cortical depression. It has been determined that neuronal reactivity of the superficial layer of the cortex is not necessary for this phenomenon. This is a curious result because while spreading depression is a dendritic like reaction in the sense that it is completely graded, a fully developed reaction probably represents the most complete depolarization the dendrite ever undergoes.

A new technic for study of the superficial cortical electrical reactions has been developed which permits much more accurate experiments, and which also permits accurate observations in drug experiments in face of extreme changes in blood pressure and which also eliminates other artifacts such as spreading cortical depression.
LABORATORY OF CLINICAL SCIENCE
Seymour S. Kety, Chief

The Section on Pharmacology under Julius Axelrod has continued its studies on the fate, metabolism, and mechanism of action of drugs which act on the nervous system with several notable achievements in the past year. In collaboration with Schmid and Tomkins of NIAMD, he has found enzymatic mechanisms in the synthesis of N-glucuronides and in the formation of bilirubin glucuronide, leading to the elucidation of a biochemical lesion in congenital non-obstructive, non-hemolytic jaundice. He has added significantly to knowledge concerning the metabolism of epinephrine by elucidating the enzymatic process involved in the o-methylation of catechols, characterizing its requirements and demonstrating it in a number of organs including the brain. He has shown that this process plays a key role in the metabolism of epinephrine and norepinephrine in vivo. In collaboration with Agranoff of NINDB, a method for the estimation of meprobamate in body fluids was developed and applied to a study of the disposition in man of this widely used ataractic agent.

The Section on Biochemistry under Marian Kies, in collaboration with Alvord of Baylor and Roboz of Georgetown medical schools, has for several years been concerned with a better characterization of the materials in brain tissue responsible for experimental allergic encephalomyelitis. In the past year they have further purified their active preparation, obtaining a protein fraction with a ten-fold increase in activity. A collagen-like material was also isolated from brain, characterized and found to have moderate activity.

The Section on Cerebral Metabolism under Louis Sokoloff has, as part of a cooperative study on aging, made a substantial contribution to the physiology of aging in their finding in over 50 normal elderly men that a decrease in cerebral blood flow is not a concomitant of the aging process. The decrease which has often been found by previous investigators appears to be limited to those with evidence of gross mental changes. These findings are about to be extended in studies at St. Elizabeths Hospital by Lassen and Lane with a modification of the technique which employs radioactive krypton as the tracer gas. The section has continued its development of techniques for measurement of blood flow continuously and locally and their application to physiological and clinical problems. The studies by Sokoloff, in collaboration with Kaufman of the Laboratory of Cellular Pharmacology, on the mechanism of action of thyroxine continue to produce promising and significant results, indicating an important effect of thyroxine on protein synthesis.
The research goal of the Laboratory is the investigation of the ways in which social processes bear upon the production and course of psychic disturbances. Included with this goal is a wide range of research areas: the nature and distribution of mental illness and behavioral pathologies, social and cultural variations in defining and treating behavioral disturbances, social and cultural patterns influencing personality development, interpersonal processes within the family, and social processes in the treatment setting of the mental hospital. This range of interests is represented in the current projects of the Laboratory.

With the growing recognition of the importance of social aspects of illness and with the realization that relationships between social and medical or biological factors are more complicated than has been assumed, there has been an intensification of research interests and efforts in conceptual and methodological issues and in collaboration across disciplinary lines.

During 1957, the organization of the Laboratory has been completed with the staffing of the Section on Social Studies in Therapeutic Settings.

Social Developmental and Family Studies

Research in this Section, under the direction of Dr. Marian Radke Yarrow, is devoted to systematic study of socialization influences at various stages of individual development. The greatest emphasis is upon the period of childhood, but critical developmental periods or shifts in social roles in adult life, such as in old age, are also considered.

The assumptions that personality is significantly shaped by the social interactions in which the individual participation from infancy on through life, and that adult outcome bears a significant relation to early experiences are readily accepted, though research knowledge has not succeeded in defining precisely these relationships or in explaining the processes by which antecedent conditions affect subsequent behavior. Advances toward this knowledge rest partly on refinements in methodology as well as on systematic investigation of research hypotheses.
Some of the efforts of the Section are directed toward methodological problems. Several scientists have begun work on techniques for obtaining more detailed and, hopefully, more valid data on the child's social learning environments. One such approach is the development of techniques for the study of the family in its natural setting, making use of direct observational data. That this is a very difficult problem is reflected in the scant research which has been done thus far in the field. A second project concerns the investigation of processes of recollection and reporting of earlier childhood and family conditions. Much of current research concerning relationships between early experience and later development rests on retrospective data; an understanding of memory changes is lacking. This factor is believed to be of particular significance in investigating retrospectively such problems as family relationships in the childhood of schizophrenics, where the recall of past events may be markedly modified by the subsequent developments.

In the investigation of family and societal influences upon the child, seldom has research given consideration to the level of the child's perceptual and cognitive understanding of the experiences to which he is exposed. That is, what are the developmental stages in children's sensitivities to and discriminations in interpersonal relationships? A project has been carried out which is concerned with the child's sensitivities to the personality, characteristics and motives of the persons with whom he interacts, and his modes of causal thinking about interpersonal relationships. Much of the analysis of these data has been completed during the past year and reporting of findings has begun.

Attention to the interplay of social and biological factors in development has been part of the focus of two of the projects of this Section, one, a study of family and community influences in the development of identical quadruplets, and the second, a study of social characteristics and problems of old age. Both projects were undertaken collaboratively with other disciplines. In both, data collection has been completed. The interrelationships between social and physiological conditions is demonstrated in the study of human aging, in a relationship occurring between various behavioral indices in the aged and the subjects' combined status on measures of $O_2$ consumption and environmental impoverishments.

The work of the next year will be devoted to the completion of the just preceding projects and to the expansion of the methodological studies described above.

Community and Population Studies

This section, directed by Dr. Melvin Kohn, studies the relationship between broader aspects of the social order and mental health or illness. The long range program includes: (1) research on social factors in the etiology of mental illness and behavior pathologies;
(2) studies of the processes by which mental illness is recognized or defined and the channels through which it is brought to treatment (whether by formal therapeutic agents or other means); and (3) studies of community organization, social structure and cultural dynamics basic to these aims.

Much of what we should like to accomplish in the first two areas is unattainable at present for lack of basic knowledge. For example, in the research done by Kohn and Clausen on social factors in the development of schizophrenia, it became apparent that further progress awaited a fuller understanding of the relationship between social class and family structure in the normal population. Therefore, for the immediate future, much of the section's work will have to be focused on problems of basic importance to social psychology. Before we can discover too much about social factors in the etiology of schizophrenia we shall have to study, for example, social variation in child-rearing practices and personality development. Basic to our understanding of the processes by which mental illness is defined and dealt with is research on the processes by which deviation from sub-cultural norms is handled. For the present, the third aspect of the long-range program is the most important.

Following a study that showed a relationship between socio-economic status, parental authority behavior, and schizophrenia, efforts have been directed toward securing more adequate knowledge of the structuring of family relationships in middle and working class families. The fieldwork on this study is now complete, as is the first portion of data analysis, a comparison of the values of parents in the two social classes. It was found that middle class parents are more likely to attach primary value to self-control, consideration, curiosity, and happiness; working class parents to obedience, neatness and cleanliness. It was also found that the parent's values vary directly related to the ways that they raise their children.

In line with the Section's interest in the processes by which mental illness is recognized or defined and the channels through which it is brought to treatment, Dr. Stephen Boggs has been developing a study of cultural differences in the ways that community resources (formal and informal) are utilized by people with problems. He has conducted preliminary fieldwork and is now in process of developing a systematic research design for the investigation.

A third study has been undertaken to ascertain the relationship between social background and drug therapy for prognosis among functionally psychotic patients. Dr. Erwin Linn has been abstracting the relevant data from Saint Elizabeth's Hospital records to be able to determine whether or not prognosis is improved with drug therapy, and to what extent patients of varying social backgrounds react differentially to drugs.
There follow summary statements of the objectives of each of the projects to which appreciable amounts of staff time were allotted during 1957.

Office of the Chief

Project No. M-3-C-1
Title: Analysis of Theoretical and Methodological Issues in the Sociology of Mental Health and Illness

Project Staff: John A. Clausen

To examine current research within the laboratory and within the larger field, searching for theoretical convergences and for problematic issues in empirical findings, especially bearing upon the relationship between social structure and personality development.

Project No. M-3-C-2
Title: The Impact of Mental Illness upon the Family

Project Staff: John A. Clausen, Leila C. Deasy, Harriet S. Murphy, Eleanor E. Carroll

To study the effects upon the family of the father's or mother's mental illness, by focusing on a limited number of hypotheses and questions raised by an earlier study within the following areas: (1) the effects of mental illness upon the personal relationships within the family and the family organization, (2) the family's understanding and perspectives of the illness, and (3) the social implications of the illness. Families under study are to include both parental and conjugal families of schizophrenic patients.

Project No. M-3-C-3
Title: The Adaptation of the Mental Patient to his Family Upon Return from Hospitalization

Project Staff: John A. Clausen, Leila C. Deasy, Harriet S. Murphy

To study the rehabilitation process following the patient's discharge from a mental hospital, in terms of two interdependent sets of dimensions: (a) the patient's progress toward mental health, and (b) the changing structure and functioning of the family of the patient.
Social Developmental and Family Studies

Project No. M-S-D-1

Title: The Formation of Children's Peer Relationships

Project Staff: Marian R. Yarrow, John D. Campbell

To investigate the process by which children form impressions of each other and develop patterns of interactions in social situations. To study the effects of developmental, personality and social factors on this process.

Project No. M-S-D-2

Title: Adult Leadership in Children's Groups: A Study of Leader's Sensitivity and Functioning in Relation to the Social-Cultural Composition of the Group

Project Staff: Marian R. Yarrow, John D. Campbell

To study the adult leader's role in children's groups, assessing: (a) congruencies and discrepancies in leader's and children's perceptions of interpersonal processes in the group, (b) bases and consequence of discrepancies between leader's and children's perceptions, and (c) leader's behavior and sensitivities regarding the individual child and the group in relation to the social class and racial composition of the group.

Project No. M-S-D-3

Title: The Validity of Retrospective Data on Parent-Child Relationships

Project Staff: Marian R. Yarrow, John D. Campbell

To study the extent to which valid information about early aspects of a child's development and parent-child relationships can be obtained from parents' retrospective reports. Specifically: (1) To assess the nature of differences between earlier events and parents' recollection of such events. (2) To determine how retrospection is influenced by such factors as the time interval between events and recall, intervening events, and the current social-psychological situation.

Project No. M-S-D-4

Title: Life-styles in Aging

Project Staff: Marian R. Yarrow, Olive W. Quinn, E. Grant Youmans

This project is part of a larger research on the functioning of physically healthy aged persons, which brings the perspectives and
measurement of physiology, psychiatry, psychology and sociology, both singly and in combination, to the examination of the problems and factors in aging. The primary objective of this part of the total research is to examine relationships between the demands and supports of the aged person's social environment and his functioning -- as it is defined in terms of the organization of his daily behavior, his planning for the future, his attitudes toward himself and his relationships with others. Environment is assessed in terms of (1) the social expectations and stereotypes imposed upon old age, and (2) the impact of common changes or crises of old age, such as retirement from employment, family losses, and social isolations.

A second research objective is the investigation of inter-relationships between the social psychological variables described above and physiological, psychiatric, perceptual and cognitive data.

Project No. K-3-D-5

Title: The Identification of Self in Identical Quadruplets: A Special Case of the Problems of Jibling Rivalry and of Multiple Status

Project Staff: Olive W. Quinn

To analyze (1) interactional patterns, and (2) incompatible statuses in a group of mentally ill identical quadruplets, in an effort to understand the individual's struggle to establish a definition of self in relation to the group. This problem is seen within the framework of stresses arising from or exaggerated by the fact of multiple birth.

Project No. K-1-J-6

Title: The "X" Family as Seen by the Community

Project Staff: Olive W. Quinn, Leila C. Deasy

This is one part of a larger study of the "X" family from the points of view of various disciplines, with the intent of deriving or exemplifying hypotheses regarding nature-nurture contributions to the development of schizophrenia. In this regard, the influences of the family on the community and of the community on the family comprise an area of information essential to a full understanding of how mental illness in the "X" quadruplets developed.

Project No. K-3-D-7

Title: Exploratory Study of Methodology for Assessing Interpersonal Relationships within the Family

Project Staff: Marian R. Yarrow, Thomas L. Gillette
To develop techniques of investigating interpersonal relationships within the family, in the natural family setting.

Community and population Studies

Project No. M-S-P-1

Title: A Comparison of the Social Relationships of Children in the Middle and Lower Socio-economic Strata

Project Staff: Melvin L. Kohn, John A. Clausen, Eleanor E. Carroll

To ascertain whether or not there are consistent and patterned differences between the social relationships of children from the middle and lower socio-economic strata of urban society.

Project No. M-S-P-2

Title: Exploratory Study of the Use of Local Community Resources for Handling Mental Health Problems

Project Staff: Stephen T. Boggs

To evolve and test hypotheses about the utilization of formal agencies and informal resources (family, friends, associates and strangers) by people with personal problems; the social factors in the community affecting this utilization; and the consequences of various ways of handling problems for the subsequent career of the individual.

Project No. M-S-P-3

Title: Pre-hospital Social Factors, Treatment with the Tranquilizing Drugs, and Behavior as Prognosticators of Successful Release from a Mental Hospital

Project Staff: Erwin L. Linn

To determine the relationship between (a) the patient's pre-hospital social background, (b) his course of treatment in the hospital (with particular interest in reserpine and chlorpromazine) and (c) his behavior while in the hospital and the duration of hospitalization and probability of readmission, for functionally psychotic patients. Among the questions to be asked are the following:
1. Are patients treated with chlorpromazine or reserpine more likely to be released during the first year of hospitalization and more likely to remain out of the hospital one year after release than a comparable group of patients admitted to the hospital before the use of tranquilizing drugs?
2. Have the tranquilizing drugs increased the probability of release of patients not treated with drugs because of the generally "calmer"
atmosphere of the hospital during the current period of drug therapy?

3. To what extent do patients of varying social backgrounds react differentially to the drugs?

Project No. M-S-1-4

Title: A Twin Family Study of Mental Deficiency

Project Staff: Dr. Franz J. Kallmann, Dr. Gordon Allen

To assess the frequency with which mental subnormality can clearly be ascribed to non-genetic factors and to elucidate the interaction of genetic constitution with environmental causes of subnormality. Also to develop better methods for the collection and interpretation of twin data in medical research.

Project No. M-S-1-5

Title: Social Mobility and the Milieu of the Psychiatric Hospital

Project Staff: Leslie Schaffer, Leila C. Deasy

The study is an attempt to explore the relevance and implications of some theoretical work by Harold Lasswell concerning social structure and social mobility—particularly his notion that there is a significant negative relationship between the extent to which a group achieves solidarity and high morale and the incidence of mobility among its members. It is hoped to clarify in theoretical terms a particular perspective concerning the value context of the psychiatric hospital and, in particular, some of the problems concerning respect as a value. Among other questions is whether there is a significant difference between the incidence and intensity of vertical mobility in a psychiatric setting as compared with conventional medical and surgical settings.
During the past year, the functions of the Section on Technical Development have been quite varied. Included are consultation on the instrumentation problems of laboratory personnel, design and development work on these problems, construction, repair and maintenance, internal operation, and administrative activities.

In the area of design and development, several items of equipment have been built as the result of a request by an investigator. Some of these, to be listed here, are potentially of widespread interest. For the Laboratory of Psychology, a device for putting discriminations on magnetic tape, and during playback, having these filtered from the sound system and used to give a visual indication. A system for communication, stimulation, and recording from within a sound-proofed room to an outer room. For the Laboratory of Neuroanatomical Sciences, a device for photoelectrically counting urine drops and reinjecting an equal amount of saline solution into the animal. For the Laboratory of Biophysics, numerous high impedance amplifiers, power supplies, data boards and control circuitry to aid them in preparing for the annual trip to the Marine Biological Laboratory in Woods Hole, Massachusetts. For the Director of Basic Research, a slave scope assembly to facilitate photography of an observed waveform on an oscilloscope. For the Laboratory of Neurochemistry, an "Automatic Sample Changer and Radiation Register" for the sequential counting of blood samples for predetermined amounts of time. For the Laboratory of Neurophysiology, a technique for mounting and using thermistors in measuring the temperature of the cortex.

The Section on Technical Development has been engaged in repair and maintenance to the limit that staffing will permit. Responsibility is naturally assumed for all equipment built by this facility, or modified by this facility. Repair of commercial equipment is undertaken when an economic saving can be effected.

Assistance is often asked for and given in the form of consultation. First the feasibility of a problem is determined and then the mechanics are worked out. This may take the form of the proper commercially available item to purchase, or it may result in a project best done by this Section, or a combination of the two. The result of consultation may also be a set of specifications that will be sent out on bid.

Internal activities include projects considered worthwhile by the Section which are pursued further on the initiative of the Section Chief. One such project is a miniaturized high voltage supply, powered by an
air jet. This will be described further in a later report. Another activity was the expansion of the Technical Development facilities which carried over into the first part of this year. Stocks were rearranged for better accessibility and work areas were made more efficient by the installation of power distribution panels at each position. Files were expanded to include the year's newest electronic equipment pertaining to medical research and continue to be available to investigators desiring to use them. Stock requisitions and equipment loans were continued to provide components and instruments to laboratory personnel on a minimal delay basis. The procurement of supplies extends well beyond the Section's own needs in order to forestall long delays when an investigator needs a component quickly.
During the year 1957 the Laboratory of Cellular Pharmacology has continued its favorable development. The Laboratory has not yet reached its maximum potential size and there has been considerable difficulty in the recruitment of technical and supportive personnel. From the standpoint of professional personnel the year has seen relatively little change. Drs. B. Levenenberg and G. Jamieson have joined the staff of the Laboratory as Commissioned Officer and Visiting Scientist respectively, while Dr. J. Durell has gone to the Department of Psychiatry at Yale University on a Training Grant from the National Institute of Mental Health. On the other hand several vacancies at the technical level have not been filled and cannot be filled because of lack of applicants. While the reasons for these recruitment difficulties are probably beyond the scope of this report they are pointed out, in the hope that some action may be possible to remedy this unfortunate situation.

Very little progress has been made as yet towards the establishment of a Section on the biology and biochemistry of medicinal plants. Developments in this area depend on the construction of a greenhouse facility which is in the planning stage. It is hoped that progress will be more rapid in the next year so as to allow us to proceed vigorously in the development of a program on alkaloid synthesis and plant biochemistry, since these areas are of great interest to a balanced program in cellular pharmacology.

The scientific efforts of the Laboratory have continued to center along three main lines:

1. Studies on biological methylation.
2. Studies on amino acid metabolism.

It has been pointed out in earlier reports that these three broad areas have been selected because of their central importance in basic biochemical research and because of their special relevance to problems of cellular and neuro pharmacology. Since the Laboratory is a relatively small and tightly knit research group, we favor close and frequent exchange at the intellectual as well as at the technical level between the various staff members. The development of an atmosphere of mutual interchange has been facilitated also by the fact that the chosen areas of study represent different facets of a broad, continuous research spectrum rather than exploration into entirely separate fields. It will be seen from the detailed analysis below that many of the projects are listed as belonging to more than one of these three areas.
Biological methylation: As has been pointed out in earlier reports, the wide biological significance of transmethylation reactions is reflected in the universal distribution of methylated compounds in great variety and at all levels of biological organization. The central role played by the amino acid methionine in transmethylation reactions has been emphasized in recent years by a series of discoveries from this Laboratory and others throughout the world. Transmethylation reactions are involved or play a part in the biosynthesis of substances of particular interest to neuropharmacology such as the neurohormones, the alkaloids and some of the vitamins and steroids.

It has been recognized that transmethylation reactions in particular, and transalkylation reactions in general, have some features which may be considered of general interest in energy metabolism and possibly cellular transport mechanisms. This might be of particular relevance to basic research in neurology since cellular transport mechanisms play such a key role in mechanism of conduction and transmission of the nervous impulse. While Projects 1, 2, 3, 4, 11, 12 and 15 contribute particularly to this general area they also contribute to other important areas of biochemical research. For instance Dr. Durell and Cantonii's studies on the synthesis of methionine by enzymatic transmethylation are of particular interest to studies of protein chemistry since the purified homocysteine thethin methylpherase has been found to undergo a sulfhydryl dependent polymerization reaction which is essentially without precedent but which is potentially of very great significance in our understanding of the cytochemical architecture of the cell.

Amino acid metabolism: A study of the intermediary metabolism of amino acids and of proteins offers great possibilities for contributions at the basic level of biochemical research and for the development of a program on cellular regulatory mechanisms. It has become increasingly clear in recent years that many among the physiological cellular regulators such as neuro hormones, polypeptide hormones, and plant hormones are derived directly from amino acids. Studies on the metabolism of amino acid are also related to comparative biochemistry because one of the characteristic features of mammalian metabolism as opposed to the metabolism of lower species is the relative inability of the mammal to synthesize amino acids. Finally, studies in the areas of amino acid metabolism are of particular interest to mental health since in numerous mental and neurological diseases there is evidence of derangement in the metabolism of amino acids. It is particularly noteworthy, in this connection, to emphasize the important contributions of Dr. Kaufman's studies on aromatic hydroxylation reactions. These studies have lead to the discovery that a hitherto unrecognized cofactor is involved in the conversion of phenylalanine to tyrosine. Much progress has been made towards the elucidation of the structure and function of this cofactor and it is of interest to note that progress at the basic level has been paralleled by increased interest in the biochemical
etiology of the disease oligophrenia phenylpyruvica, a disease which is characterized by a genetically determined inability to metabolize phenylalanine. Dr. Kaufman's important contributions have advanced our understanding of the disease and contributed greatly to the general area of neurochemistry.

Another area of research which relates, in part at least, to amino acid metabolism is protein synthesis. In the course of the last year the Laboratory has developed a major interest in this relatively new area of research, and is gradually attempting to find its own experimental approach to it.

At the present time it appears possible to make a fruitful beginning at an enzymatic level by studying systematically the various steps which are postulated to occur between free amino acids and a completed biologically-active protein. In reality only the very initial phases of this complex sequence of reactions can be visualized and studied in detail and it is hoped that as progress is made the next steps will become clearer. The overall problem is a most difficult and challenging one, for proteins are the most complex and fragile polymers known in nature. The problem of protein synthesis is intimately related to the problems of protein structure, of biosynthesis and function of the nucleic acids, and less directly to the challenge of biochemical genetics, chemical morphology and biological evolution.

Although practically all of the work of the Laboratory deals with amino acid metabolism in general, Projects 5, 6, 7, 8, 9, 10, 13 and 14 contribute more directly and specifically to this field.

Comparative biochemistry: As was pointed out in earlier reports, the relationship of comparative biochemistry to cellular pharmacology is one of the foundations of the scientific philosophy of this Laboratory. A research program in comparative biochemistry can be developed favourably through a long term general interest supplemented with intermittent specific contributions.

Thus implications for comparative biochemistry constitute a recurring, albeit minor, theme in many of the projects which can be specifically classified as contributing to the problem of protein synthesis, aromatic hydroxylations, enzymatic transmethylation, etc. More directly pertinent to comparative biochemistry are Dr. Mudd's studies on the MAE in yeast and Dr. Jamieson's studies of sulphate utilization in Chlorella as are Dr. Kaufman's studies on the metabolism and enzymology of phenylalanine in man.
BIOMETRICS BRANCH

ANNUAL REPORT FOR CALENDAR YEAR 1957

General

The Biometrics Branch has made continuing progress in each phase of its program which consists of the following activities: (a) collecting, processing, and analyzing data on the extent of the problem of the mental disorders, particularly with regard to patients under treatment in mental hospitals, in outpatient psychiatric clinics, in general hospitals with psychiatric services, and in public and private institutions for mental defectives and epileptics; (b) providing consultative services to State research bureaus on the organization of statistical services on the design of follow-up, evaluative and other special studies; and (c) providing consultative services on design of experiments, analysis of experimental data, development of mathematical models to the other Branches and laboratories of the Institute, particularly to personnel engaged in basic and clinical research.

During the year a reorganization of the Branch was carried out in line with recommendations made in the recent Manpower Utilization Study of the Branch's activities. The Current Reports Section was subdivided into three separate sections so that the Branch now consists of the following: Hospital Studies Section, Outpatient Studies Section, Consultation Section, Section on Applied and Mathematical Statistics, and Community Studies Section.

The Branch has made considerable progress in the collection of data on patients under treatment in mental hospitals and clinics. Nevertheless, the task of collecting data on the fate of patients admitted to such facilities remains an extremely difficult task because of the lack of certain essential knowledge on the etiology and epidemiology of the mental disorders and the absence of instruments that can be used in comparable fashion from institution to institution to determine severity of illness and to characterize the psychologic status, the degree of psychiatric disability, social and familial adjustment and physical condition of patients at various intervals following onset of disease. As more new therapeutic programs (drugs, use of day and night hospitals, half way houses, open hospitals, etc.) and treatment facilities are introduced into hospital and community programs, the task of obtaining data on people under treatment becomes increasingly difficult and complex, and data derived from separate treatment facilities, such as public mental hospitals and clinics and psychiatric services in general hospitals, become increasingly difficult to interpret. It has become quite apparent that state mental health and state mental hospital authorities must develop statistical reporting programs that will coordinate basic data on patients under treatment in all known psychiatric treatment facilities in their jurisdictions and will include appropriate follow-up data on the various classes of patients. The Branch has been working with states to improve reporting within public mental hospitals and clinics. This job
is far from complete and we plan to continue our work with states to improve hospital and clinic reporting, to develop methods that will reflect changes resulting from new treatment programs and concepts. In addition we will intensify our efforts to devise methods for collecting coordinated data on patients under treatment in all psychiatric facilities within defined geographical areas.

The Branch is also taking steps to program certain of its operations for the IBM electronic computer. The availability of this machine will make it possible to produce more quickly certain data on patients under treatment in psychiatric facilities and to permit more detailed and rapid analysis of certain types of data involving computation of decrement tables, rates, correlation coefficients and other types of computations.

The services of the Section on Applied and Mathematical Statistics continue to be in increasing demand by the investigators in the basic laboratory and clinical research programs of the National Institute of Mental Health. Through an arrangement with the Biometrics Branch of the National Institute of Neurological Diseases and Blindness, this section also provides similar services for the scientists of that Institute. This section has carried out its own research activities developing several new techniques in multivariate analysis which are helpful in the analysis of profile data and in the analysis of variation. The Section intends to provide liaison services between investigators in laboratories and branches of NIH who plan to collect extensive data and personnel in NIH developing programs for the electronic calculator scheduled to start operating at NIH during 1958. This section is also contemplating the possibility of initiating investigations into mathematical biology and information theory because of the significance of such research in various aspects of the mental health field.

The Community Studies Section has not, as yet, been activated due to difficulty in recruiting a staff, particularly a person to direct its activities. Active attempts will continue to recruit appropriate personnel for this important aspect of the Branch's activities.

A problem that makes the achievement of results in the biometrics field slow is the shortage of well-qualified personnel to fill positions both in the National Institute of Mental Health and in the field. Not all states have bureaus of statistical research within state departments of mental hospitals and mental health, and only a few of the states with these departments have well-trained people. To improve this situation at least two things are needed. First, directors of state mental hospital and health programs must be willing to give strong support to the development of adequate statistical research programs. Second, they must be willing to pay salaries at a sufficiently high level to attract well-trained and imaginative people into the field. Third, steps must be taken to increase the pool of trained analytic and mathematical statisticians to fill the increasing need for such personnel in action and research programs in the mental health field. The NIH has taken steps to attempt to alleviate the shortage, starting a grant program designed to develop training centers for biometricians throughout the Nation and for giving fellowship support to promising students.
The major part of the Branch has been separated from the National Institutes of Health reservation for somewhat more than two years. Although the office space in the Perpetual Building is satisfactory, there are still many problems involved in developing an efficient office arrangement because of the separation of the offices over three floors of the building and the fact that even on the same floor all offices are not contiguous. The staff in the Perpetual Building feels keenly the separation from the Institute because of the lack of frequent contact with the professional and other personnel in the various branches of the Institute and the lack of contact with personnel in the other Institutes on the NIH reservation. The Chief of the Branch spends a fair amount of his time traveling between T-6 and the Perpetual Building to attend executive staff and other meetings on projects in which the Biometrics Branch has a definite interest. The Branch hopes sincerely that steps can be taken in the not too distant future to bring it back onto the NIH reservation.

The reports of the individual sections follow:

HOSPITAL STUDIES SECTION

During the year the Hospital Studies Section continued its work in further developing the Model Reporting Area for Mental Hospital Statistics, carrying out cooperative studies with individual hospitals and state mental hospital systems on methodology of cohort studies and developed new techniques needed to gather information which would permit more meaningful analyses of trends in the movement of mental hospital populations.

Seventh Annual Meeting of Mental Hospital Statisticians. The 18 states in the Model Reporting Area held their 7th Annual Conference in Washington, D.C., in May 1957. The conference concentrated on interstate comparisons of cohort studies giving probabilities of first significant release during the first 12 months following admission, re-evaluation of basic definitions of patient movement terms, and the need for more specific annual and monthly data on the movement of patient populations in mental hospitals.

Cohort Studies. Implementing a recommendation of the 1956 meeting, 11 states completed cohort studies in which groups of first admissions in specified age, sex, and diagnostic groups (schizophrenia and mental disorders of the senium) were followed during each of the first 12 months of hospitalization to determine probabilities of release, death, or retention. The data showed considerable variation among states in release, death, and retention rates for each category of patients. A committee reviewed these findings during a meeting in January 1957 and developed a list of factors which might account for these differences, such as screening facilities in the community, legal requirements, administrative policies, type of patient admitted and severity of illness. The committee recommended that these cohort data be published including data from each state that might make it possible to partial out the effect of some of these variables and
emphasizing the problems inherent in interstate comparisons of mental hospital data. The Conference approved the recommendations of the committee and the Section staff is now preparing these data for publication.

It is significant that eleven states have now carried out these studies when as recently as five years ago no valid measures of mental hospital release rates were available on a statewide basis.

The Biometrics Branch has continued to work with the Warren State Hospital, Warren, Pennsylvania. Data are being obtained that will make it possible to analyze the experience of cohorts of first admissions to this hospital during the period 1916-55, not only by age, sex, and diagnosis but also by such variables as urban-rural residence, occupation, marital status, therapies, etc., and to determine readmission rates to the hospital after specified periods of time following release by these variables. It is expected that some analysis of the data for the period around 1950 will be completed within the next few months.

The Branch continued its cooperative study with the Department of Mental Hygiene of the State of Virginia of first admissions to state mental hospitals of that state over the period 1952-55. Cohorts of released patients will also be studied to determine probabilities of return to the hospital within a specified number of months after release. In order to obtain a more adequate base for computing such probabilities, a search of the death certificates in the Virginia Department of Health is being carried out for all patients released alive from the hospitals. This will also permit the computation of death rates within specified periods of time after admission regardless of whether the patient died in the hospital or outside of the hospital. Preliminary analyses have indicated some very interesting differences between the various age, sex, and racial groups.

Another cooperative study with the California State Department of Mental Hygiene on the experience of first admissions to the Pacific State Hospital during the five-year period, 1949 to 1953, was completed during the year. The study was the first cohort study ever conducted on patients admitted to institutions for the mentally deficient. The findings indicate that there were striking differences in release rates by age, I.Q., and diagnosis. For patients with I.Q. under 20 only 7% were released within 4 years following admission, whereas for patients with I.Q. of 70 or over, 72% were released within 4 years. Among patients in the age groups 14-17 years, 60-70% were released in the first 4 years, while among those under 5 years of age, only 12% were released. Patients with diagnoses of undifferentiated or familial mental deficiency had release rates of 55-60%, while those with diagnoses of mongolism and developmental cranial anomaly had release rates as low as 10-15% but had high death rates of 27-28%. A paper incorporating the methodology and results of this study was prepared cooperatively by the Biometrics Branch and personnel from the Pacific State Hospital and was presented at the annual meeting of the American Association for Mental Deficiency in May 1957. The results of this study have served as a starting point for a more intensive research
project on the factors influencing the prognosis in mentally deficient patients admitted to Pacific State Hospital. The National Institute of Mental Health is supporting this research through a special grant.

**Trends in Public Mental Hospital Populations.** A study was carried out in which the movement of patient populations in public mental hospitals in 1956 was compared to what would have been expected on the basis of the trend over the period 1945-1955. While the analysis of the gross data indicated that the number of resident patients in public mental hospitals of the nation at the end of 1956 was lower than would have been expected on the basis of the trend in the period 1945-1955, data needed to assess the factors responsible for this decrease were not available. The gross hospital data on the movement of patients must be made specific for such basic variables as age, sex, diagnosis, and length of hospitalization, etc., and state mental hospital systems have, with minor exceptions, never developed techniques to produce such tabulations. The section developed a method to solve this problem using data at Saint Elizabeths Hospital to determine release and death rates among groups of patients according to such variables as age, sex, diagnosis, length of stay, marital status, race, and type of commitment. It is planned to work with several other states to develop similar analyses so that more adequate interpretation of interstate comparisons of trends in mental hospital population movement can be made. Indeed, this study emphasized that obtaining the facts necessary to quantify the impact of tranquilizing drugs and such other therapies and programs as may be developed in the future on the mental hospital requires the revision of existing statistical systems in mental hospitals to provide appropriate intrahospital data. But equally as important, programs must be developed which will coordinate data on utilization of all community treatment facilities so that the role played by the mental hospital can be studied in relation to that played by these other community facilities in the treatment and rehabilitation of the mentally ill.

**Monthly Reporting.** Monthly reporting of gross public mental hospital population movement by the states in the Model Reporting Area was begun in December 1956 to obtain mental hospital population movement data on a more highly current basis and to see whether striking changes are occurring, to consider the effect of seasonal variation in the analysis of changes in the movement of these populations. Examination of the data collected during the first 10 months indicates considerable variation in the movement of these populations from one month to the next and also considerable variation among states. However, until data have been accumulated for more than one year it will not be possible to determine what proportion of the change from one month to the next is due to seasonal variation and what proportion is due to other factors. Such information will begin to emerge during early 1958.

**Mortality Studies.** Tabulations of the number of deaths occurring in public mental hospitals in 1955 were made available to the Biometrics Branch by age, sex, mental disorder, and cause of death by 17 states in the Model Reporting Area. An analysis of the data is presently under way, using the IBM 650 computer, to determine age and cause specific death rates,
percentage distributions of deaths by cause and the ratio of hospital
deaths and death rates to deaths and death rates in the general popu-
lation. Preliminary findings indicate a marked variability in the distri-
bution of causes of death between the various age, sex, and mental
diagnostic groups and considerable variation by state. However, certain
patterns do emerge. Deaths due to arteriosclerotic and degenerative
heart disease account for the greatest percentage of all deaths, with
deaths from pneumonia the next highest. As would be expected, over 3/5
of all deaths occurred in the age group 65 years and over. The death
rates in the mental hospitals are higher than the corresponding rates
in the general population.

In addition to studying the death experience of the mental hos-
pitals of the 17 states, this study provided valuable experience in the
programming of vital statistics calculations on the IBM 650. This ex-
perience will be particularly useful in programming data for the pre-
paration of the annual census of patients in mental institutions.

The Third Midwest Conference on Mental Health Statistics. This
conference was held at Lansing, Michigan, in October 1957. Much of the
discussion centered around a refinement of interstate comparisons of
gross data on mental hospitals and institutions for the mentally deficient
in the Midwest. In addition, the following were among the topics dis-
cussed: analysis of mental hospital population data; measures of effective-
ness of hospital programs; recommendations for consideration by the
Committee on Definitions of the Model Reporting Area and reports of
research projects in the various states. These meetings are an outgrowth
of the annual meetings of the Model Reporting Area and since representa-
tives from midwestern states who are not members of the Model Reporting Area are
also invited, interest in sound statistical procedures in mental hospitals
has been stimulated in these states

CONSULTATION SECTION

The objectives of the Consultation Section are to establish
efficient records systems, to promote use of comparable terminology and
definition, and to facilitate data reporting and data analysis. Imple-
mentation involves providing consultative services in setting up a records
and reports system or reorganization of out-moded and cumbersome records
systems.

By furnishing advice and assistance in research design and data
analysis, the Section not only aids in procuring much needed information
but stimulates other states to engage in research by establishing working
models, methodological techniques, and, occasionally, resources.

The following states requested and received consultative services
regarding improvement of their central office, mental hospital, or out-
patient psychiatric clinic records systems or on matters regarding research
design, program evaluation, and data analysis: Delaware, Florida, Georgia,
Kentucky, Maine, Massachusetts, Michigan, and Ohio.
Specific examples of assistance furnished by the Section upon request of state or local mental health agencies or facilities are briefly presented below:

The Institute in Jackson Memorial Hospital, Florida, and the clinic attached to Tampa General Hospital, Florida, requested assistance on developing methods to furnish the Biometrics Branch with the data requested annually. The problem stemmed from the fact that the out-patient psychiatric clinics were part of a generalized medical care program and the record systems used in these clinics were part of the total hospital record system. A plan was devised for incorporating a form for psychiatric clinic data into the basic record system.

Assistance was given to the superintendent and staff of South Florida State Hospital with regard to setting up a records and report system. The request was unique inasmuch as it was tendered by the superintendent before the official opening of the hospital. Consultation in this case was particularly satisfying since discussions regarding a records system were unencumbered by an existing records system.

At the request of the superintendent of Pineland Hospital and Training Center, Maine, a school for the mentally retarded, their current records and reports system was reviewed. The superintendent was interested in establishing an IBM machine punched card system to be used for administrative and research purposes. A statistical system utilizing an IBM key punch and card count sorter with schedules, coding and punching instructions was provided for his use.

Consultation services were also provided to the Kentucky Department of Mental Health and the hospitals they supervise in the revision of its records and reports system. This reorganization was to a large degree prompted by their desire to qualify for admittance to the Model Reporting Area. This state has applied for admission to the Area.

Several projects on the evaluation of drug therapy in the hospital setting and in a home care program were reviewed with the Clinical Director of the Delaware State Hospital and members of his staff. Suggestions regarding use of cohort methods in analysis of follow-up data were made. Discussions were also centered about the use of concurrent and historical controls in clinical trials. A form was designed to be used in a visible file register to guide follow-up of patients and to present information rapidly on the status of patients in the project.

The Chief of the Research Section of the Michigan Department of Mental Health requested advice on the collection and analysis of research data on patients under treatment in the hospitals and clinics of that state. Among the studies that were reviewed were ones on rates of first admission to their hospitals and another on the evaluation of the public health nursing services to the families of hospitalized mental patients and to the patients themselves when they are released to the community.

Consultative service was requested by the Georgia Department of Health in relation to the evaluation of two programs. One program involved public health nursing services to families of the mentally ill;
the other program pertained to general hospitals providing diagnostic and treatment facilities for the mentally ill. The former program had been in operation for several years. The problem was to devise forms and set up procedures which would enable them to collect certain basic data that would enable them to ascertain to what degree such services were being utilized as compared to an optimum utilization. Reasons for low utilization in given areas could then be investigated. Modifications in the existing methods of collecting data and in maintenance procedures were made which would permit the above requested administrative information to be readily collected. Further recommendations were made concerning the collection of individual patient and family data for research purposes.

So as to insure some built-in evaluation techniques into the other program, the state department of health requested consultation in the planning stage in order to include items which might indicate the degree to which the program objectives were being met. Briefly stated, these objectives were to reduce the number of patients going to the state mental hospital from counties participating in the program, to return such patients to the community more quickly than could the state mental hospital and decrease the number of readmissions. Since randomized controls which would permit direct evaluation of these objectives was not feasible, several other approaches in analyzing the accomplishments of the program were suggested. These measures would throw some light on shifts in patterns of hospitalization for communities with and without such mental health facilities. Some revisions in the data forms and data collection procedures were made. Models for data presentation and analysis were also presented.

The Chief of the Section is also supervising a contract study being done by the Harvard School of Public Health for the Biometrics Branch. This study will determine probabilities of release and return using two different points in time ("significant" release or return and "standard" release or return) for cohorts of admissions in the years 1900, 1940, and 1950. The follow-up period is limited to five years after admission and will consider such variables as age, sex, mental diagnosis, education, marital status, etc.

The 1900 cohort has been coded and punched and some preliminary analyses have been made by age, sex, and type of admission (first and readmission) for 1) entry hospital, 2) legal status, 3) marital status, 4) birthplace, 5) occupation, 6) education, 7) usual type of household, 8) place from which admitted, 9) in hospital during year preceding admission, 10) cause of death. A detailed cross-tabulation by age, sex, diagnosis, and type of admission was also made. These analyses formed the basis for determining how to group certain variables and which cross-tabulations would be practicable for the more detailed analysis.

The Section also reviewed the records system of the Ohio Department of Mental Hygiene and Correction. As part of this review, data on first admissions during the years 1948-1952 are being correlated with pertinent 1950 census information enabling the computation of admission rates by such factors as age, sex, color, marital status, education, occupation, resident (urban-rural, metropolitan-non-metropolitan, county),
mental diagnosis, etc. Proximity to state mental hospital facilities and the effect of other mental hospital facilities on admissions to state-operated hospitals is being considered. A portion of the findings will be presented in a regional research conference to be held in Ohio early next year. Subsequently, data involving discharge and readmission will be analyzed.

OUTPATIENT STUDIES SECTION

Activities in this year have concentrated on the analysis of the data being reported in the annual statistical reports from out-patient psychiatric clinics and providing assistance in extending reporting of information on patients to an increased proportion of the clinics in all states, furthering the standardizing of definitions, putting into effect the plan that is to provide the National Institute of Mental Health for research study, duplicate standard punch cards that include data on each terminated patient, and on the development of a plan for a special study on the socio-economic characteristics of clinic patients in 1960.

A comprehensive analysis of data on clinic characteristics and the number and type of clinic staff and man-hours reported by 95 percent of the 1,234 clinics in 1954-55 was completed and is being published in December 1957 as a Public Health Monograph.

"A Manual on Recordkeeping and Statistical Reporting for Mental Health Clinics" has been published and is being made available to Regional offices, states, and clinics.

A resume of the workshop on "Concepts in Mental Health Reporting" at the annual meeting of the American Orthopsychiatric Association was published in the Journal of the Association and reprints made available for distribution to the states by the National Institute of Mental Health.

The subcommittee on Reporting of Diagnostic Classification for Children attended by representatives of the American Psychiatric Association Committee on Nomenclature and Statistics, American Orthopsychiatric Association, and several other child guidance clinic representatives and representatives of the Children's Bureau and other branches of the National Institute of Mental Health met on September 12-13 to discuss problems on reporting diagnoses for children.

Data on the patients and services they received in outpatient psychiatric clinics for about 380 clinics were reported for the year ended June 30, 1955. The reporting clinics, comprising about one-third of the total number of clinics in the country, do not represent a probability sample of all clinics and generalization from the findings cannot be made to the total clinic patient population in the nation. These first reports on the characteristics of patients and their services, however, provide within this important limitation some preliminary information on patients. Briefly summarized, some of these data show the following:
1. Of each 10 patients terminated during the year, 3 received diagnosis and treatment, 4 received diagnosis only, and 2 had received other services only, that is, only an application interview, partial evaluation, psychological testing, etc.

2. The bulk of the terminated patients - about 8 of each 10 - left clinic service after less than 10 interviews with a professional staff member. More than 2 in 10 had only one interview, and almost 4 in 10 had 2 to 4 interviews.

3. When the patient was an adult, most interviews were with the patient; only 1 in each 10 interviews was with a spouse or other person about the patient. When the patient was a child, only half the interviews were with the child patient; 4 in each 10 were with the parent or parent substitute, and 1 in 10 was with some other significant person about the patient.

4. Not quite a fourth of the terminated patients, either because they came for services other than diagnosis and treatment or because they did not continued their visits, were undiagnosed when terminated. For children with a psychiatric disorder, transient situational personality disorder was the most frequent diagnosis - 36 percent. Personality disorders (21%); mental deficiency (18%); and Psychoneurotic disorders (13%) also comprised fairly large groups. Among the patients 18 years and over with psychiatric disorder, personality disorders (29%); psycho-neurotic disorders (28%), and psychotic disorders (24%), were most prevalent.

5. The 1955 data on patients made possible for the first time an estimate on total patients using outpatient psychiatric clinic facilities. On the basis of the number of clinic patients served per man-hour of professional staff time in the reporting clinics and earlier reports on man-hours of service in all clinics, it has been estimated that 197,000 patients under 18 years of age and 166,000 patients 18 years of age and over used clinic service sometime during the year ended June 30, 1955, in continental United States. These very rough estimates provide a clinic usage rate of 355 for each 100,000 population under 18 years of age and 155 for each 100,000 population 18 and over.

Data on patients for the year ended June 30, 1956, were reported for almost 500 clinics—about 100 more than reported for 1955, and these represent about two-fifths of the 1,294 clinics in the United States in 1956. These reports are being processed for tabulation and analysis. Of the reporting clinics, 237 also prepared special tables that provide additional detailed information on some items and cross tabulations of other data that will make possible a more complete analysis of the data for 1956.
The uniform duplicate punch card plan designed to provide data on each terminated clinic patient to NIMH to facilitate national research was put into effect. Thirty-six states with punch card procedures are participating in the program. Approximately 100,000 cards, that is, data for 100,000 patients terminated during the year ended June 30, 1957, in 477 clinics will be received by NIMH during the last quarter of 1957. Plans are being made for taking national samples of patients with selected characteristics for special analysis. Plans are being considered for additional studies to be made in cooperation with the states in order to obtain further information on these patients. Present plans include the submission of duplicate standard punch cards again in 1960.

Plans are being developed for the collection of information on socio-economic characteristics of patients admitted to clinics for a specified period in 1960 to be related to the population census in 1960. To date 20 States have indicated an interest in participating in such a study and additional states are expected to indicate interest; 5 have reported that they cannot participate. Some of the socio-economic characteristics of patients for which information may be collected are education, employment status, occupation, income, mobility, urban-rural (and census tract) residence, marital status, nativity, family size and composition, housing, etc. The data will provide rates of admission from the various socio-economic groups as well as relationships between socio-economic characteristics and diagnosis, outcome after treatment, services received, number of interviews, etc.

SECTION ON APPLIED AND MATHEMATICAL STATISTICS

During the year the section has continued to assist and consult with investigators on statistical, mathematical, and biometrical problems arising in various investigations carried out by the laboratory and clinical scientists at NIMH as well as scientists who are working in mental health problems outside NIMH. These services provide the scientists with the most efficient and valid statistical techniques available in the design and analysis of data. The section has been consulted on a large variety of subjects including experiments on the effects of various drugs on psychiatric and sociological functions in animals and in man; investigations in electrical conductivity, sections and resections, and vascularity of nerve tissue; studies in reaction time; continuous performance tests on various groups of people; surveys on interactive patterns among socio-economic groups and among the emotionally disturbed; and continuous consultation has been provided to the multidisciplinary aging project.

The section has developed new techniques in mathematical statistics especially in multivariate analysis which are helpful in the analysis of profile data and in the analysis of variation. Advice has been provided to various committees with regard to grants, surveys, and proposals in the field of mental health. The Section has also reviewed manuscripts arising within the Institute and has served as referee on papers submitted for publication in statistical journals.
The section proposes to continue consultations with these investigators already begun and to continue to aid the Psychopharmacology Service Center to obtain definitive evaluations of new drug therapies in mental illness. Next year we intend also to provide liaison services between investigators in the laboratories and branches of NIMH who plan to collect extensive bodies of data and the machine programmers of the electronic calculator which has been procured for NIH. The section is also contemplating the possibility of initiating investigations in mathematical biology and information theory because of the significance of such research in various aspects of the field of mental health.

In addition to providing a variety of statistical and mathematical services to research and clinical investigators of NIMH, this section has also been called into consultation by investigators outside NIMH working in mental health. These services include consultations in the design of experiments, the analysis of data, and mathematical models underlying the data. The section has served on and provided advice to various committees in NIMH as well as reviewing and refereeing papers in the disciplines involved in mental health.

Some examples of the investigations in which this section has participated by providing consultations in design and analyzing data are:

1. Experiments on the effects of various drugs on psychological functions in animals and man.
2. Experiments on the effects of certain nerve sections and resections.
3. Studies of various social and psychological relations in socio-economic groups.
4. Studies on a maternal attitude test.
5. Ecological investigations in animals.
6. Investigations of blood vessel density in various spinal neural regions.
7. Studies in the methodology of behavioral observations.
8. Reaction time experiments in normal controls.
10. Comparison of brain damaged with normal groups on Continuous Performance Tests.
11. Leadership studies in childrens camps.
12. Survey on job satisfaction at NIH.

ACTIVITIES OF THE CHIEF OF THE BRANCH

During the year, the Chief of the Branch engaged in certain activities that might be noted. He was invited to lecture to the students and faculty of the Department of Public Health of Yale University and to conduct a seminar on problems of research in the epidemiology of mental disorders. He was also invited to participate as a member of a study group convened by the World Health Organization in Geneva from November 4 to 8 to consider problems of the use of ataractics and hallucinogenic drugs in psychiatry. While in Europe he was also invited to lecture at the Institute of Psychiatry of the University of London at the Maudsley Hospital on the collection of data on the mentally ill in the United States, geographical variations in the availability of psychiatric personnel and facilities, and the other activities in which the Biometrics Branch has been engaged.

He also participated in the following conferences: 1) A conference on patterns of patient care called by the Joint Commission on Mental Illness and Mental Health, Boston, March, 1957. 2) Conference on coordinating community resources in psychiatric after-care sponsored by Pennsylvania Mental Health, Inc., Philadelphia, April 1957. 3) Conference on research in mental health sponsored by the Florida Conference on Training and Research in Mental Health, April 1957.

The Chief of the Branch has been designated to provide liaison between the National Institute of Mental Health and the Epidemiologic Intelligence Service Training Program at the Communicable Disease Center in Atlanta, Georgia. In this connection he presented a paper at the May conference of the EIS and lectured to a training class of EIS officers during August 1957 on problems of research in the epidemiology of mental disorders. The NIMH is supporting this training program, and it is hoped that through our active participation we will attract some of the trainees into epidemiologic research on the mental disorders.

The Chief was also asked to confer with the personnel responsible for the mental health training and research program being implemented by the Southern Regional Educational Board. In this connection he reviewed types of data that are available on the prevalence of mental disorder and distribution of personnel and facilities in the seventeen states that are members of the Board and made recommendations concerning the development of adequate statistical services within the state mental health programs of that region, the training of medical record librarians, and the need for extensive studies within the states of that area to throw greater light on regional differences in the utilization of psychiatric facilities.
The Chief of the Branch provides liaison between two special grants being carried out in the California State Department of Mental Hygiene and the NIMH. The first project, a study of suitability of out-patients for treatment was completed in 1957 and a report has now been published on this study by the California Department of Mental Hygiene. This report has been issued as Research Report Number 1 of the California State Department of Mental Hygiene.* The second project is being carried out at the Pacific State Hospital at Pomona, California. This project includes both an extensive research program investigating individual, familial, and community factors related to admission to and release from the institution, and evaluating the effect of specific treatment and rehabilitation programs within the hospital on the prevention of disability and the training of patients for community employment. In addition, this project is being used as a training center to attract into the field of mental retardation high caliber research personnel in psychology, psychiatry, biometry, sociology, and epidemiology.

Both the Branch Chief and the Chief of the Section on Applied and Mathematical Statistics serve on the Psychopharmacology Advisory Committee.

A list of the publications of the Branch follows.

Publications of the Branch


Hospital Studies Section, Mental Patient Data for Fiscal Year 1956. Public Health Reports, Volume 72, Number 1, January 1957.

Hospital Studies Section, Patients in Mental Institutions, 1953, Part III: Private Hospitals for the Mentally Ill and General Hospitals with Psychiatric Facilities. PHS Publication No. 495, Part III.

Hospital Studies Section, Patients in Mental Institutions, 1953, Part IV: Private Institutions for Mental Defectives and Epileptics. PHS Publication No. 495, Part IV.

Hospital Studies Section, Patients in Mental Institutions, 1954, Part I: Public Institutions for Mental Defectives and Epileptics. PHS Publication No. 523, Part I.
Hospital Studies Section, Patients in Mental Institutions, 1954, Part II: Public Hospitals for the Mentally Ill. PHS Publication No. 523, Part II.

Hospital Studies Section, Patients in Mental Institutions, 1954, Part III: Private Hospitals for the Mentally Ill and General Hospitals with Psychiatric Facilities. PHS Publication No. 523, Part III.

Hospital Studies Section, Patients in Mental Institutions, 1954, Part IV: Private Institutions for Mental Defectives and Epileptics. PHS Publication No. 523, Part IV.

Hospital Studies Section, Progress in Reporting Mental Hospital Statistics. Public Health Reports, Volume 72, Number 9, September 1957.


Biometrics

BUDGET SHEET

Estimated Obligations for FY 1958

Total: $329,253

Direct: $316,478

Reimbursements: $12,775
Previous annual reports have described in considerable detail the rationale for the current organization of the Clinical Investigations program. Our research efforts have been directed on the one hand toward improvements in treatment methods for a variety of psychiatric disorders, and on the other toward making contributions to a better understanding of the factors which influence normal personality development and behavior. Certain studies from each of the branches and laboratories were described in order to indicate the scope of their research, and particularly the areas in which collaboration between several disciplines was involved.

In the four and one-half years since the first ward was opened to patients, the general areas of interest of each research group have gradually been defined. These are still subject to change, depending as they do upon developments in the field, on the nature of the Clinical Center setting, and on the special skills of the staff. Nevertheless, all the branches have by now decided upon one or more major projects to which they have committed their resources. The main portion of this report is devoted to descriptions by their chiefs of the activities of the branches and laboratories.

During the past year we have been fortunate in the appointments of outstanding investigators to fill the two major staff vacancies. In September Dr. Joel Elkes reported as Chief of the Clinical Neuropharmacology Research Center, which is being developed in collaboration with St. Elizabeths Hospital. Dr. Elkes was Professor of Experimental Psychiatry at the University of Birmingham, England, where he initiated a remarkably well-integrated program of psychiatric research ranging from the psychological to the anatomical bases of behavior. At the end of December at the termination of his fellowship at the Center for Advanced Study in the Behavioral Sciences, Dr. David Hamburg will come as Chief of the Adult Psychiatry Branch. Prior to his fellowship, Dr. Hamburg had served as Associate Director of the Institute for Psychosomatic and Psychiatric Research and Training of Michael Reese Hospital. Both Dr. Elkes and Dr. Hamburg have made significant contributions in their special fields; in addition, they are particularly interested and experienced in the problems of interdisciplinary research; and, finally, they are unusually competent administrators who have demonstrated their ability to achieve a high standard of research sophistication while at the same time maintaining a sensitive and effective clinical operation.
Although it will obviously take at least two or three years for Drs. Hamburg and Elkes to build their branches to a state of maximum efficiency, there are many immediate advantages which result from their arrival. They bring to the group of laboratory and branch chiefs who are responsible for the development of the Clinical Investigations program the much-needed resources and the unique points of view gained from their wide clinical and general research experience. Further, it is now possible for the first time to make long-term commitments of the clinical facilities which it will be their responsibility to operate. This will open the way to a whole range of studies within the clinical branches themselves and in collaboration with others, which have hitherto been held in abeyance or pursued on a more or less intensive pilot basis.

In a sense, we can say that the first phase in the organization of Clinical Investigations is nearing successful completion. We now have within the group strong representation of the various disciplines which we conceive to be necessary for the further development of theories of behavior and of personality development. Although later we should like to see our clinical facilities expanded to include a small therapeutic community-type hospital and a child institute, we already have in the Clinical Center and in St. Elizabeths Hospital access to reasonable flexible facilities which will enable us to set up many situations for critical study. We are at last nearly ready to essay an answer to the question of how best to organize and utilize these personal, professional, material, and structural resources.

It should be made clear that we recognize that there are areas of autonomy for each of the behavioral sciences, and we assume that certain advances will be possible only after further progress in the individual disciplines. But in any review of this total field it does appear that the areas between disciplines have been relatively neglected, and our unique resources for collaborative studies impose upon us a responsibility to pursue them where there is reason to believe that they might be profitable. Even a cursory scanning of the reports which follow will indicate that up to the present time we have, at best, carried out some multidisciplinary rather than interdisciplinary research - that is, in some studies representatives of various disciplines working side by side have collected data in certain experimental situations. This I regard as a step in the right direction, and I believe that we have done about as well as could be expected. In the early life of most groups there is first the formation of a number
of sub-groups. Not only do the members of these sub-groups tend to identify strongly with each other, but there is often a tendency to exclude those who do not share their point of view. With varying intensity this has occurred among our branches and laboratories. To some degree the breaking down of these barriers will reflect the success the group of laboratory chiefs achieve in finding some common ground.

Circumstances related to the necessity of starting a clinical operation before some of its key personnel were appointed have resulted in two types of administrative organization within Clinical Investigations. Some of the branches contain representatives of various disciplines: Child Research, Clinical Sciences, and the Clinical Neuropharmacology Research Center. Others are largely unidisciplinary: Adult Psychiatry, Psychology, and Socio-Environmental Studies. The advantages of the unidisciplinary type of organization are that it facilitates strong identification with one's own discipline; evaluation of proposed projects or of work in progress is apt to be more sound; observations made in one area of the group's concern are readily correlated with data gathered in others. A potential problem of this type of organization, however, is that it may foster a relative lack of that type of commitment which is absolutely essential in a clinical project where treatment responsibilities are assumed in order to afford research opportunities.

The multidisciplined branch does not have this problem of commitment to the project; and since all of the investigators are responsible to the same chief, the organizational lines for efficient operation are clear. This may make for the earlier effectiveness of such a group. On the other hand there is a definite tendency to in-group formation with the resulting loss of contact with others in the larger operation who are similarly engaged. Sometimes in the interest of promoting mutual goodwill potentially productive differences are ignored; each discipline becomes too "understanding" of the others; the special competences of each tend to become blurred; and the level of performance may sink to the lowest common denominator in a setting where a pseudo-equality becomes a goal.

I do not believe that such problems as these can be legislated out of existence by adopting a particular pattern of organization. A continuing alertness to their development
is essential to their resolution, and our ultimate success will depend on our frankness and our willingness to face them when they do arise. But these are matters for the future. The current status of our work is reported in the following pages by the chiefs who are responsible for the development of the studies in which we are engaged.

Robert A. Cohen, M. D.
Director of Clinical Investigations
National Institute of Mental Health
For the Adult Psychiatry Section working on Ward 3-W, the past year has on the whole been transitional; it has involved the rounding off of previous phases of research and the planning of a new program which will be both more focused in research objectives and more varied and expansive in the approaches used to reach these objectives. The program of this ward, viewed in over-all perspective since the opening of the Clinical Center, has now completed a rather distinct evolutionary stage. The program began with a rather large number of psychiatrists using the ward individually for quite numerous and heterogeneous projects. This permitted a considerable variety of fruitful pilot studies, but a shift to a more consolidated program seemed to have three major advantages: those studies which are continued can then have a larger and more adequate sample of patient material, more focused staff participation permits a more inclusive and thorough penetration into questions which are particularly significant; and the clinical operation of the ward can be more readily integrated with the research.

Arising out of ongoing research on this ward has been a heightened conviction that a crucially strategic area for increasing our understanding of mental disorder lies in the examination of family relationships. This conviction is in accord with general clinical and statistical studies from a half-dozen countries which have repeatedly confirmed the finding that schizophrenics emerge almost exclusively from severely disturbed homes—a finding which provides perhaps the most consistent lead concerning etiology that has been found in any kind of investigation of schizophrenia. In addition, early familial experience has long been accepted as a pivotal factor in determining personality development and deviation. However, it is only recently that the details of how this generalization applies to the genesis of schizophrenia has begun to be subjected to systematic research scrutiny.

Research in this section has led to a preliminary specification of the nature of these familial influences in the development of schizophrenia. This research has progressed from clinical observations and an intensive pilot study of five
families of schizophrenics to the formulation of a series of hypotheses which can be summarized as follows:

1. The parents of potential schizophrenics have had serious difficulties in their own personality development in achieving a sense of personal identity— that is, a self-concept in which they can clearly differentiate themselves from others and which they can maintain over time in a variety of relationships. Clinical observations indicate that difficulties in identity formation and threats to one's sense of identity provoke intense anxiety and strenuous efforts to reduce the impact of such anxiety.

2. One way of dealing with such personality strain is for the person to seize upon an interpersonal relation that can have the continuity that personal identity lacks. Obviously, the parent-child attachment offers an opportunity for such a relation during the child's growing years, especially if the child is relatively passive and malleable for "constitutional" reasons. The need to maintain such a relation in a particular form acquires all the emotional intensity that is ordinarily associated with the maintenance of personal integrity and identity.

3. Such relations, like all others, become structured through interactional processes into particular complementary or reciprocal roles. In relations of the quality and intensity described, deviations from expected roles have come to represent a threat of explosive anger and recrimination.

4. The intense need for a sense of relatedness, together with the threat of its disruption, leads to a particular kind of relationship in which open recognition of even ordinary, inevitable divergence from expected roles is strenuously avoided. The resultant quality of relatedness has been summarized in the concept of pseudo-mutuality. Pseudo-mutuality involves a characteristic dilemma: divergence from expected roles is perceived as leading to disruption of the needed relation, but if divergence is avoided, new ingredients that would permit growth of the relation and of the individuals' personalities are excluded.
5. In the families of potential schizophrenics, it is hypothesized that pseudo-mutuality of an especially intense and enduring form characterizes the acknowledged family relations. Legal members of the family may be psychologically excluded from the internally acknowledged family role structure as it is perceived by the rest of the family who are involved in pseudo-mutual relations. However, the resultant quarrels and schism between the acknowledged family and the ostracized legal family member may be highly functional for the organization of the family as a whole as seen by an outside observer, who can regard the scapegoating of someone as essential to the continuity of the pseudo-mutuality in the rest of the family. In other instances, other persons or events outside the family may be scapegoated as a way of avoiding recognition of internal family divergence. In still other instances, legal outsiders, such as hospital personnel, may be psychologically incorporated into the family pseudo-mutuality and role structure in order to facilitate its maintenance for a time.

6. In addition, in the families of potential schizophrenics, it is hypothesized that the intensity of the necessity of maintaining pseudo-mutuality has led to the development of a particular variety of shared, family mechanisms by which deviations from the family role structure are delusionally re-interpreted or excluded from open recognition. Further, the effectiveness of these mechanisms is enhanced by a pervasive familial subculture of myths, legends, and ideology which stress the dire consequences of openly recognized divergence from a relatively limited number of fixed, engulfing family roles.

7. In the families of schizophrenics these shared mechanisms act at a primitive level in preventing the articulation and selection of any meanings that might enable the individual family member to differentiate himself from the family role structure. It is hypothesized that the resultant patterns of interpersonal perception and communication become a part of the offspring's personality structure and involve a kind of fragmentation and confusion of
experience and thought which is a central feature of schizophrenia. Also the offspring has come to develop only those ego skills which have been valued within the special constrictions of the family role structure, leading to a personality impoverishment that becomes clearly apparent when the offspring needs to assume extra-familial adult roles.

8. Further, it is hypothesized that different family members will occupy different positions or roles within the family social organization, leading to differing consequences for the personality development of the offspring. (This hypothesis has been confirmed by a detailed examination of very extensive material on a family in which the offsprings are monozygotic quadruplet schizophrenics.)

In the planning of further empirical research in this section, these hypotheses have served as a fruitful focal point. The section planning has been interdisciplinary, with the participation of psychiatrists, social workers, nurses, sociologists, and psychologists. More recently, a committee consisting of Dr. Lyman C. Wynne of Adult Psychiatry as Chairman, with Dr. Joseph Handlon of Psychology and Dr. Leonard Pearlin of Socio-Environmental Studies, has been working out a specific research plan for consideration by the total staff which will be taking part in the ward program.

The intent in this research is to examine three especially significant unsettled problems: (1) The degree of constancy of familial disturbance in schizophrenia in relation to such variables as: type of schizophrenia, age and type of onset, family social class, and kind of family constellation; (2) The degree of specificity that some aspects of family disturbance may have for schizophrenia, or for varieties of schizophrenia, compared to the generality of some other features of family disturbance which may also occur normally or in other disorders; (3) The question of the extent to which the family disturbance is a primary factor in the development of schizophrenia or, alternatively, a secondary consequence of the individual's pathology.

The implementation of this long-range program is at present planned along two main lines: (1) Intensive studies on Ward 3-W of the family relations of schizophrenics and, in comparison studies, of neurotics. Current plans include the trial, in a variety of settings, of a group therapy approach to each
family as a whole, the use of quasi-experimental family group test procedures, and the detailed evaluation of the extent to which features of family interaction carry over to the individual family member's relations with others, especially in observed ward behavior; (2) Extensive studies, off the ward, of a larger and more varied sample of families, including "normals", in order to check specific items in statistical comparisons. Such work, interdisciplinary but with a sociologic emphasis, has been usefully considered in over-all planning, even though it will not be operationally practicable to proceed with it until the more intensive studies have been advanced.

In September 1957, Dr. Charles Savage departed for a year's leave of absence, after having completed a number of papers on his studies of psychodynamic processes in the therapy of schizophrenics, especially the effects when therapy is conducted in a research setting and when the patient receives psychotomimetic and tranquilizing drugs.

Despite the emphasis upon family studies for the future, certain investigations which have continued to seem valuable and which do not use separate inpatient material are to be extended; a study of the extent to which social mobility of various professional groups contributes to difficulties in interdisciplinary collaboration; a study of role conflicts in the clinical investigator arising from the difficulties of integrating research and therapy values; the development and clarification of the role of psychiatric ward administrator; the linguistic study of emotional expression; and the effects of certain perceptual and imaginative impairments upon learning capacity, for example, in reading.
Adult Psychiatry Branch  
Section on Ward 3-E  
Dr. L. Murray Bowen

General Statement

The work of the section is devoted almost entirely to one project, the title of which is "The Study and Treatment of Schizophrenia as a Family Problem." It is anticipated at a later stage of development that there will be several projects in the section.

This project was started thirty-eight months ago to bring normal family members into a living situation in the Clinical Center with hospitalized schizophrenic patients. This was considered a potentially rewarding area for study. It is well known that there is a vigorous emotional process when a psychotic patient is in living contact with his family. A theoretical plan had been worked out which, it was hoped, would make it possible for the families to live in the hospital setting for indefinite periods, and also for it to be a practical and possible venture in the Clinical Center. The intensity and specific characteristics of the intense emotional conflict between the family members had not been anticipated in the plan. Clinical experience was that the conflict between family members could transfer itself into a conflict between staff members. This transfer took place in the context of ordinary treatment relationships between staff and family members. Changes in both the theoretical formulation and in the treatment approach were made during the first two years. The changes went toward finding families in which the tendency to transfer their problems to others would be less, and in developing concepts and techniques to help the staff to work with the families without becoming involved in the family problems. The immediate motivation for the change was to make the clinical operation into one that was liveable and operable both for families and for staff and that also seemed to offer some hope for treatment successes. While these changes were empirical and made in service of the clinical situation, they had also a direct bearing on the theoretical formulation. By the end of the second year, the ward operation seemed to have reached a controllable and workable level. No further changes have seemed indicated since that time. The plan includes fathers, mothers, and patients as the minimal family group for study. Schizophrenia in the patient is regarded as a symptom manifestation of an active process that involves the entire family, and the family therefore treated as a unit.
A characteristic of the operation has been the difficulty in making accurate predictions of the project course. For instance, each year there has been an impression that the project staff had reached a workable capacity to deal objectively with the emotional problems of these families. Each time staff again encountered an unexpected situation which required further resolution. One error in predication seems to have come from the application of criteria from individual psychotherapy to the work with the more intense and involved family group problem. Another error has been the lack of experience with family groups and the fact that it has not yet been possible to follow a family through to completion of treatment.

The year 1956 ended with a fairly stabilized clinical operation. There were no upsets between staff and families that could not be understood and controlled within a few days. This stabilized period was seen more as a calm period between crises than the beginning of a sustained controlled clinical operation.

**Developments and Trends in 1957**

The year 1957 is seen as a transition year for the project. This was the first year in which there were no major changes in either the hypothesis or treatment operation. The more stabilized clinical operation, which began in 1956, continued throughout 1957. The clinical operation was much more able to "run itself." Clinical problems required less time and a corresponding increase in staff time was devoted to efforts to more accurately structure and define the research problems.

The first efforts to perceive the family as a unit began as a clinical necessity. When a staff member related individually to a family member, it could be the point at which the family problem could become transferred to an intra-staff problem. It is believed that "family unit" concept made it possible for staff to see the family in a different way than would have been possible observing fathers and mothers and patients. The presence of the family group in a setting where they could be observed constantly provided a source of detailed objective data that would be hard to obtain in any other setting. Many promising observations were marked "for future study" and passed over during the early stages when the main effort went to stabilizing the clinical operation. Early in 1957, when there was more time for research efforts, some of these areas were
selected for detailed study. The effort was not successful. The details seemed out of place in the absence of more precise overall concepts. The effort was then directed to a more detailed thinking through of the overall project. This resulted in four papers written during the year. The result of this has been far from satisfactory. Another effort is now being made to define some of the more specific observations.

Progress in 1957

The changes in the project have the characteristics of a growth process in which it is difficult to describe a change as belonging to one period. Some patterns do stand out. There are three principal areas of activity and interest, all interdependent. This includes relationships within the family group, relationships between family and staff, and relationships within the staff. An interference in one area has a potential of showing almost immediately in all three areas. Interference in staff-family relationships seriously threatened the project during the first year. There was careful structuring of the conditions under which staff members would relate to family members the second year. This brought enough control over staff-family relationships to stabilize the clinical operation and to make possible more accurate observations in the intrafamily area. The focus of research observations during the second year was on relationship patterns between family members. The third year the main changes have been in intrastaff relationships. A year ago very strict structuring was still necessary to prevent staff-family relationships from involving the operation in an undefinable emotional turmoil. As the staff began to understand itself better, the structure became more of a natural process than a necessary set of rules.

The staff effort to understand intrastaff relationships has been accompanied by a much clearer perspective of the family as a unit. There was a beginning perception that the family unit had group characteristics just as the individual has individual characteristics. The evolution in the staff seemed to permit enough detachment from the individual to see the family.

The concept of the family as a unit may be one of the more important concepts in the project. There are events in the family when the activity, the intentions, or even the attitude in one member can set up changes in another member.
An example is the mother who developed physical illnesses in response to a change in her daughter. When one's interest and focus is on the individual, there is a much greater tendency to see the family in relationship to that individual than to see family relationships as a phenomenon. The development of psychotherapy for the family group was also developed as a clinical necessity but it appears to have some advantages over individual psychotherapy that are worth exploring.

Another major clinical change in 1957 was developed to deal with a clinical problem. The interchange between psychic and somatic problems is intense in these families. Over a year ago the project assigned itself the task of combining psychotherapy and general medical care within a single physician. This has brought into focus a number of problems previously missed when psychic and somatic problems were divided between two physicians. To handle the anxiety situation, the physician who operates the two areas has gone in the direction of structuring medical practice in a psychotherapy frame of reference. This area has presented a number of promising clues for further study.

The following outline by Dr. Warren Brodey illustrates concretely some aspects of the narcissistic relationships and reality testing observed during the study of these families.

**Family-Staff Mechanisms**

1. The staff and family by the nature of this study maintain close proximity. It is necessary for family and staff to negotiate with one another in dealing responsibility with such situations as, obtaining a pass to leave the unit, periodic physical examination, passing food at the dinner table, etc. These families were chosen because of the primitive intensity of their intra family relationships. It has been found that this intensity readily spills over into family-staff relationships, and that even simple negotiations frequently break down in an atmosphere of intense family-staff emotions. This capacity to evoke powerful responses in others is historically a characteristic of these families.
2. Examination of this process of evocation in the family-staff relationship indicates a specificity in the positions that are assumed by the staff members in relation to the family. These positions, when compared to the intra family roles, are seen as "stand-in" positions--the drama being reenacted is tradition for each family, and has been called the family mythology. This mythology has a control axis or leitmotif along which all the parts are played, i.e., good-evil, powerful-weak, praised-criticised, competent-incompetent, sick-well, etc. Autonomous stimuli from staff members or other extra familial figures are responded to in terms of this central axis--the degree to which this occurs is directly related to the degree of lack of coincidence of the stimulus with expectation and the level of anxiety that prevails. The process of putting the autonomous stimuli or the person emitting them into line, is called polarization.

3. Examination of this process of polarization indicates that the family responds so as to reinforce the possibility of getting in return a response closer to its own projected expectation. This is accomplished by the fragmentation of the total reality into accurately perceived parts, and then utilizing for response these accurately presented parts, without reference to their relationship to the whole or each other, i.e., with altered perspective. Thus a statement is responded to in terms of its symbolic meaning without reference to its reality component, as a long term generalization with reference to its immediate intent, etc. The staff member who responds to the fragment is pulled toward the axis of orientation of the family member. The alteration of perspective in the staff member is a subtle process. It is often effective in altering the orientation of the staff member in the direction of the family mythology, particularly as it is made clear that this is the only way to obtain or maintain relationship.
4. The concept of circular causality if found useful in considering the effect of the above noted process, in the creation of an altered reality. Thus conflict (A) in the family evokes the response in the staff (B) which is closely related to the mythological expectation of (A). The response in the staff (B) then reinforces the validity of the projection of the conflict (A). This process of creating an altered reality which is valid in fact, as well as in keeping with the family mythology, is called the process of externalization.

Intrafamily Mechanisms

1. Each family has a specific set of family roles. These roles are not specific to the individual family members though one member may habitually play a particular role. Family members can trade roles with each other provided that the constellation of roles remains unchanged.

2. The roles can most obviously be described in terms of the central axis or leit motif of the family. Each role embodies a major extreme position such that persons interacting from these positions will reenact the issues of the central conflict.

3. Grossly at least, the issues of these central conflicts embodied in the family mythology are readily related to the major deep and highly energized unconscious conflicts in each family member. But the conflicts highlighted in the central axis, the leit motif, and the major roles are those conflicts which in addition to being in each individual, interlock between important individuals.

4. The major structure of these families can be viewed as the result of a process of externalization, similar to that observed in the families' relationships to staff. One can observe the same evocation, polarization, and fragmentation of reality occurring within the family as was seen in staff-family relationships. In observing the family in ordinary operation it is harder to be aware of the externalization process for it is so pervasive. In the families, externalization is facilitated by marriage choice, child-rearing practices, etc. Though ongoing process of externalization is not as readily seen - the
previous findings point up that the externalization of internal conflicts has taken place. Also, when an individual family member, perhaps through his therapeutic work, makes an effort to introduce into the family relationships aspects of himself which do not coincide with the image projected from other family members, then the processes which maintain externalization are observed to become more evident.

Considering the above observations the intense close relationships apparently between family members can be seen as relationships based on the cathexis of that part of the other family member which coincides with the projections from self and is essentially then not removed from self except to acted out mirror reflections. The term narcissistic relationships seem specifically descriptive of this phenomena.

5. In practice this system of narcissistic relationship is maintained by the suppression of recognition for relationship purposes, of autonomous behavior which does not coincide with the family mythology. Each family member is related to by the others in terms of the part of this person symmetrical with the role in which he is cast. It is considered that autonomous behavior other than than symmetrical as noted above is not given a negative relationship value, but rather has no relationship value.

6. There is observed a strict, iron-clad rigidity about these families. It is considered that this is related to the need to suppress spontaneity but more specifically in these families. An important characteristic is the single-minded pursuit of concrete reality and corollary abhorence of irrationality. It is considered that this inability to directly deal with irrationality has much to do with the effort to alter reality to make the irrational rational, and when this fails, to project and externalize this conflict setting up the role in the family mythology of the irrational one, the other family roles then being reinforced as the super rational ones. The role of the irrational
one is habitually occupied by the family member who manifests the psychotic symptomatology. It has been observed that the processes clinically manifest in the symptomatology called schizophrenia are an accurate caricature of the same processes which are covert within the family.
Creation and Operation of a New Research Facility

A considerable amount of staff work during 1957 went into the planning and opening of the new Children's Treatment Residence and into the exploitation for research of unique observational possibilities that offer themselves only during such periods of transition from one setting to another. While in terms of the research projects reported on in the annual report of 1956, this heavy refocussing of research effort during 1957 constitutes somewhat of a detour, for the long range objectives of the research at the Child Research Branch it probably constitutes one of the most important moves forward.

The purposes served by the Residence are:

1. To make possible the collection of research data on child patients when they have reached a level of recovery that makes their treatment in a closed hospital ward setting inadvisable, while they are not yet ready for full return to life in the open community.

2. To explore the nature of the therapeutic milieu, including social structure and staff roles, that are required during this phase of treatment and to compare it with the nature of environment most conducive to treatment in the earlier phases in a closed ward setting.

3. To create concepts which will enable us to describe the movement of patients into an improved state of mental health in terms as specific as one is now able to use for the description of their pathology while still more fully in the grip of "mental disease."

The Research Operations which were carried out in 1957 and which were closely related to the opening of our new research facility, the Residence, were the following:

1. Study of a group of "Normal Controls" - matched in I.Q., age, social background, and racial distribution with our patient group, while exposed to a week's life in the residence. Narrative recordings by staff and participant observers as well as more rigorously planned recordings by trained observers using systematic observation techniques, were used as methods in this study.
2. Study of a group of children of nursery school age with symptoms of aggressive acting out during eight weeks on 4-East, after the patients had been moved into the residence. These children were exposed to a planned summer-nursery school program while under study and the material gathered on them should permit comparison with similar behavioral expressions observed during two very different developmental phases.

3. Study of child patients on 4-East - eight children of an age range around eight years, brought in for the purpose of a temporary stay on the ward for differential diagnosis, for a limited period of observation, with two objectives in mind:

a. widening the clinical data on children with similar symptoms by studying a larger number for shorter periods of time; and

b. selection of a group of new long-range child patients with a high degree of homogeneity in a number of variables, to be chosen on a more thorough basis than the usual forms of direct intake into the ward would otherwise allow.

Operation 1. and 2. were discontinued after the end of the summer; operation 3. will continue for the rest of the year.

The exploitation of the data gained during this period and comparisons with data gained on previous control normals, as well as on our long-range patient group, is now being worked on but is not yet at a stage of completion which makes a detailed report possible.

Abstract of selected research activities as contained in the Project Reports for 1957.

Individual Therapy and Psychopathology

While two children have been without a therapist since July 1957, intensive recording has been done on the other four, who are being seen four hours a week in individual therapy. While much of this is still in the process of ongoing data collection, the materials available now for the development of hypotheses of the children's pathology, as well as for the basic trends in problems of technique, are being worked on by the therapists, their consultants, and other research staff. Comparisons of later phases with data produced in earlier stretches of therapy, organized collation of therapy data with observations gained from other sources, including the more strictly designed research projects, and with data gained about the pre-history of the children, are among the tasks on which part of the effort of research staff is being focussed at this time.
Tentative findings:

Psychopathology:

1. Hyperaggressive children display a pathology which combines aspects from childhood neuroses and psychoses to constitute a special syndrome. Although individual children differ in aspects of this syndrome, in all cases there are profound ego disturbances centering around problems of impulse control, and particularly around the control of aggression. The ego disturbances are reflected in conceptual lacks, learning difficulties, disturbances in conceptions of space and time, low tolerance for frustration, hyper-distractibility by environmental props, readiness for contagion, paranoid-like suspiciousness and projections. Despite these features, the children being studied here differ in many features from psychotic children. In particular, they do not show the autistic behavior and fantasies of the latter, they are generally in communication with the environment, and under special circumstances they show marked ego-intactness.

2. In all cases oral themes seem to play a major part in the underlying fantasies of these children. The children seem to interpret experiences via orally incorporative or destructive modes. Even material that seems initially to be predominantly phallic in tone, can be readily seen as a developmental phenomenon superimposed on an anlage of primary oral concerns.

3. Related to the above, one finds in these children intense anxiety over the possibility of dependency, and intense defenses erected against both behavioral and fantasy expressions of dependency. With progress these defenses seem to diminish both in behavior and in fantasy productions.

4. All of the children show severe problems in the formation of a sense of identity. These problems seem related to the absence of or failure of figures who might serve as transmitters of cultural or subcultural values. In all cases there is absence of a father, failure of the father to fulfill a role that might provide a source for social identification, or inadequacy of the father as communicated to the child through the mother's perceptions. With all children the opportunity for establishing any relationship (even an anti-social one) with a social order seemed lacking.
Problems of Technique

1. Foremost among these is the broad observation that, contrary to beliefs popular in the field, individual psychotherapy with the hyperaggressive child is more like than unlike psychotherapy with other categories of disturbed children. As in all cases where ego development is weak or distorted, there is, especially in the early phases of treatment, greater necessity for the therapist to function as an auxiliary ego for the patient than is true in more classical neurotic cases; this, however, is no more than a difference in emphasis, since it is well known that child therapy always requires that the therapist play a partially educational role more than does adult therapy, by virtue of the fact that no child's ego is fully formed.

2. A second impression is that the therapeutic process, while similar in course, is more prolonged than is the case with other kinds of children.

3. Third, while limit setting plays an important role in all child therapy, it becomes particularly significant in treating children whose most crucial problems lie in the area of control, fear of loss of control, and distrust of the adult's dependability and integrity in controlling both himself and the child. Since fear of seduction (in both the narrow sexual meaning and the broader sense of seduction to impulsivity of any kind) plays a major role in the psychodynamics of these children and seductive experiences often figure prominently in their history, it becomes a vital problem for the therapist to avoid confusing the wish to demonstrate his benevolent intent with seduction. Particularly in the earlier, more disorganized phase of therapy (which may be prolonged for many months and even a year or more), it may be a disquieting experience for the therapist to find himself responded to as though he were a dangerously hostile figure, and it is easy to become unwittingly seductive in the effort to correct this projection.

4. Many countertransference problems also have become apparent in this project. While the particular content of the countertransference will no doubt vary with the personality of each therapist, all those participating here have had to deal with feelings aroused by the need to meet such explosive barrages of raw destructiveness and with those aroused by the underlying oral demandingness of such children, whose own fantasy certainly seems to be one of eating up the therapist.
5. Impressions are beginning to emerge as to specific interpretive techniques. In the earliest phases of treatment, when these children communicate largely through gross motor behavior and acting out, it seems necessary to accompany the traditional resistance interpretations with fairly concrete behavioral responses to the child; it is as though actions speak loudly while words at best mean little or, at worst, signify oral sadistic attack to this kind of child. Later, as the child moves into a phase of more symbolic communication, the interpretations also seem to need to shift; at this phase communication seems best to be achieved by corresponding symbolic gestures on the part of the therapist, much as one answers a schizophrenic child's fantasy communications within the framework of his own fantasy rather than by interpretive translation. It seems only to be in the more advanced phases of therapy, as the child becomes able to verbalize directly about himself, that the weight of the interpretive effort can be shifted to direct discussion of the child's problems and their origins and remain effective. While all three levels of communication are present throughout therapy, there is a difference in their relative usefulness at various phases.

Milieu Therapy

Under this heading are summarized a variety of research activities. The "level" on which research is carried on in this specific aspect varies all the way from naturalistic styles of data collection, the production or organized research data as part of projects with a special design and focused on limited variables and the development of concepts to the formulation of theories and hypotheses preparatory to later more rigorous selection of variables. Without going into detail the following highlights may be given special emphasis:

Tentative findings:

Concept of Milieu and Breakdown of Variables

1. It is possible to isolate about thirteen to fifteen distinct and relatively independently researchable sub-units of the milieu which seem to have behavioral impacts on the children under study.

2. At least seven quite distinct meanings are customarily invoked when the adjective "therapeutic" is attached to the milieu concept, each one of them relevant in its own right, but in need of sharp separation for the utilization in an organized research approach.
3. A considerable list of properties of games, materials, props, tools involved in activities such as arts and crafts, etc., can be isolated as of clinically distinct importance, and the therapeutic variation of these factors can be described in a considerable amount of detail. Effects of some techniques of employing such activities and of handling child behavior during the process can be distinctly seen as differing in their effect on the children from others, so that the groundwork for a more organized pharmacopoea mentioned as one of our objectives, can be seen to emerge. Such factors as have been isolated by now can be described in sufficient detail and precision to make them teachable to others and approachable in sharper research design in later studies.

4. Techniques for the clinically geared observation of surface behavior on the spot can be developed so that they avoid the traditional gap between observable surface data on the one hand and depth-psychological dynamics on the other more successfully than in the past.

Life Space Interview

Copious material collected for the purpose of exploring and structuring this technique, described in 1956, has been added to. A preliminary formulation of basic theory and technical principles were submitted for discussion to professional groups at the 1957 Orthopsychiatric Conference; parts of this are in the process of publication in the American Journal of Orthopsychiatry.

Tentative findings:

1. The variety of purposes for which treatment staff uses Life Space Interview techniques can be ordered around the following sub-goals which emerge most frequently in in-patient treatment of children with aggressive disturbances:

   a. Clinical Exploitation of Life Events, under which distinct categories have been temporarily singled out under the following labels: (1) reality-rub-in, (2) symptom estrangement, (3) revitalization of numb value areas, (4) new tool interpretation, (5) manipulation of the boundaries of the self.
b. Emotional First Aid on the Spot with subcategories temporarily classified under the following code labels: (1) drain-off of frustration annoyance, (2) communication maintenance in moments of relationship decay, (3) support for the management of panic, fury and guilt, (4) regulation of behavioral and social traffic, (5) umpire functions in decision crises and in cases of loaded transactions.

2. In terms of exploration of Criteria for the indications or contraindications of holding Life Space Interviews in a given situation, and of the choice of a specific technique, the following 6 subcategories of areas of major relevance have emerged:

a. central theme-relevance  
b. ego proximity and issue clarity  
c. role compatibility  
d. mood manageability  
e. timing  
f. impact of terrain and props.

3. On the basis of preliminary work a number of similarities were found between techniques employed by interviewer in Life Space and in Play Therapy Interviews. Among the differences in the techniques employed in the two types of interviews were the following:

a. As expected, play is used less frequently in Life Space Interviews.  
b. Techniques of control were used more frequently by Life Space Interviewers.  
c. While there were no differences in the amount or specific techniques of interpretation used in the two types of interviews, there were differences in the direction of interpretation: In Play Therapy Interviews interpretations were directed more frequently toward impulse, whereas in Life Space Interviews interpretations aimed relatively more frequently toward resistance and defense.

Learning Disturbances

The major objective of the research on Learning Disturbances carried on at the Child Research Branch is to arrive at a sharper differential diagnosis between those disturbances of learning which are intimately linked-up with the basic pathology of the children and those which are a result of previous learning failures or of important behavioral or cognitive learning blocks.
In order to isolate the variables that go into the success or failure of a specific learning task and which make a given learning situation either destructive or supportive for the learning process, our study focused especially on the problem of motivating the children toward learning activities, of exploring the type of "situational ingredients" at work and of assessing the nature of certain specific learning disturbances that seem to occur with frequency in the type of hyperaggressive child patient under study here. School records distributed over a 27 month period were sampled, rated in terms of variables involved, and later reliability was checked by use of judges not connected with NIMH. Changes in school behavior of 6 children were studied by comparing ratings for two halves of the sample by time. Clinical analyses were undertaken on the learning problems of each child and on special sources for anxiety in both, children and staff, with respect to the learning situation. With the new group of child patients on 4-East, methods are being developed on the basis of the previous studies and are focusing around the following:

1. Planned variations of school program to provide examples of behavior in different settings (individual, group; formal, informal), with different materials (verbal, manual-manipulative, etc.), and different content.

2. Participant and non-participant observation.

3. Analysis of observations to isolate variables and to develop systematic methods of describing the variables.

Tentative findings:

1. A behavior Rating Scale, which can be used reliably in judging school incidents for adjustment behavior, was developed.

2. Over the period of 27 months the children changed significantly in the direction of better school adjustment.

3. Categories for describing clinical factors accounting for school behavior and behavioral change were developed, and it was demonstrated that they could be used reliably in judging school incidents. The clinical factors in the learning situation can be subsumed under three major categories:

   a. Self (self picture; inner pressures and forces; infantile needs and frustrations)

   b. Relationships (to adults; to peers)

   c. School (subject matter, methods, material; teacher personality.)
Behavioral Measurements and the Assessment of Change

An important part of our research effort has always been geared in the direction of better methods for observing and describing child behavior and toward the development of categories of recording that would make it possible to catch the clinically relevant issues of "change." Several studies in that line were reported previously. During 1957 several additional methods were tried. Among the studies undertaken during this year are the following:

1. Systematic observations in a variety of settings and coding of individual interactive behavior during two treatment phases.

2. Systematic observations done on a control group of children, matched for age, I.Q., race, socio-economic status.

3. Categorization derived for detailed descriptions contained in clinical records and case conference materials.

4. Periodic interviews and collections of clinical incidents from Child Care Staff.

5. Exploratory interviews with child care and therapy staff directed at staff's concept of change and improvement and matched with their actual statements about observed functioning of their patients.

Tentative Findings:

Among them is one, especially, that makes it possible to list "findings" gained so far, as a result of investigations by means of the Leary-Ossorio technique which were made in two series, a year and a half apart, and from which the following suggest themselves:

1. Changes in behavior interaction patterns. From the investigation of two series of observations made a year and a half apart, the following major conclusions can be drawn:

   a. The interpersonal behavior of the children has changed considerably in the course of treatment.

   b. Over the period there is a decrease in inappropriate behavior toward peers. Most children show a trend toward more friendly peer relationships.
c. Changes in relations with adults are much more marked than changes in relations with peers. Hostility toward adults decreases considerably. Particularly there is a decline in hostile-dominant behavior and an increase in friendly-passive behavior toward adults, with a major increase in trusting, dependent expressions. Inappropriate behavior also decreases considerably. The distinction between behavior toward peers and behavior toward adults gets sharpened.

d. The behavior that the children evoke from others shows corresponding changes. Children are less hostile than they were in response to a particular child. Adults show an increase in the proportion of friendly, giving, supportive behavior with the children.

e. Different behavioral settings produce different qualities of interpersonal behavior.

f. There is an interaction between person and situation that goes beyond what either contribute independently to our ability to predict behavior. That is, although there are generalizations, settings also operate differentially for different children.

g. The effects of settings differ in the two phases. Tentatively, it would seem that in the later phase of treatment the situation comes to play a greater role as a determinant of behavior than it did previously.

h. Changes in interpersonal behavior appear more readily in some settings than in others.

i. A paper on some of these findings was presented at national meetings and is in process of publication. Data analysis is near completion and another paper is being worked on.

2. Concepts of Improvement:

a. Formulations of clinically relevant concepts of improvement are undergoing continuous change as our study proceeds, and temporary findings are as yet too volatile to be reported this year.

b. A pilot study for the collection of data on the staff's concept of improvement as related to our present child patients is in a state of partial completion. Preliminary impressions indicate that the children have improved in a number of areas. Especially, hostile interactions between children have decreased and acceptance by the children of staff interventions has gone up. Other details about improvements are too varied from child to child or require too much background data to be summarized here.
Next Step Plans

The activities reported on here are not really to be considered as a number of research projects with relatively independent objectives. They are, with some exceptions, more in the nature of a research program rather than a sequence of projects.

During the next years it is intended:

1. To bring to a state of closure those phases of the program and to finish up those studies which are in the nature of relatively limited "project type" investigations and to publish them in form of a paper or article for a scientific journal during 1958 or 1959.

2. To pull out of the larger material such sections as can be reasonably closed out as independently reportable findings and to publish them as articles or books. Among these, some will be on the level of articles in scientific periodicals or books on therapy techniques directed primarily toward the research field. Others, by the very nature of the program will combine research findings with directives to be used for staff training or for application by practitioners in the field of Psychiatric In-Patient Treatment of children, and will be addressed to each of the disciplines involved in psychiatric Residential Therapy.

3. In order to fulfill the major objective of the research program, namely the study of the treatment process during its full duration from hospitalization back to reinstitution into normal community functioning, several groups of children with similar pathology will be taken through their full course of therapy. This is a condition sine qua non for coming closer to the task of creating diagnostic concepts which will either verify our hypothesis that these child patients constitute a specific nosological entity. If the findings should come out in terms of a preference to maintain them as if a "borderline" category, to fill this category with enough specific content to make prescriptions and predictions more reliable and to separate them more sharply from borderline cases of other types. We plan to use the next years for the completion of this task.
The Clinical Neuropharmacology Research Center, now in the process of being established as a joint project between the National Institute of Mental Health and Saint Elizabeths Hospital, is a Clinical Laboratory intended primarily for the study of the action, and the mode of action, of drugs on mental function in man, with special reference to their bearing on problems of mental disorder.

The location of the Center at Saint Elizabeths Hospital was thought appropriate for a number of reasons. In the first place, it was felt from the outset that such a program would gain greatly by being initiated and maintained in a large modern mental hospital, where abundant and varied clinical material would make for the conduct of controlled large scale trials of pharmaco-therapeutic agents, as well as the ready selection of suitable case material for special intensive investigation of individual conditions and syndromes. Furthermore, it was thought desirable to expose the investigators working in the field to the, in many ways unique, phenomena presented by mental illness in a mental hospital; and thus familiarize them with the special research problems presented by a mental hospital population. Equally, it was hoped that the contact of the clinical staff of the Hospital with scientists working amongst them would make for a more ready appreciation of the role of each in a common research program. The Saint Elizabeths setting, with its long tradition of clinical care and teaching, and its high standard of resident staff therefore seemed to provide a unique opportunity for the pursuit of such collaborative research into the biology of mental illness. Its location within the Washington area, and within ready access of the Clinical Center will make for ready interaction between it, and the resources and special services of the Clinical Center. Essentially, therefore, the functions of the CNPRC and the work of other laboratories at the Clinical Center are envisaged as complementary and interdependent. It is, in fact, planned that a number of long range programs will be conducted with the active and sustained collaboration of the laboratories of Clinical Science, Psychology, Adult Psychiatry, Socio Environmental Studies; the Biometrics Branch of NIMH; and the Psychopharmacology Service Center. The full yield of the scheme of necessity hinges on the degree and the intimacy of this interaction.

A further feature which, with increasing experience, may grow in importance may be the steady definition and growth of methodological tools specially adapted for the study of large mental hospital populations and their interaction with the community. It is hoped that, in time, courses in Research Method in these special fields will emerge
as a direct outcome of collaborative studies between CNPRC, Saint Elizabeths, and the appropriate laboratories of NIH.

For the present, three broad Sections are envisioned for the CNPRC. These are the sections of Clinical Psychiatry, Chemical Pharmacology and Behavioral Sciences. Only the broadest indications of the programs of each can be given at the present stage.

1. SECTION OF CLINICAL PSYCHIATRY

One of the early functions of the Section of Psychiatry will be a systematic survey of the existing population of Saint Elizabeths Hospital, with special reference to the assessment of the impact of pharmacotherapies on the existing services of the Hospital. It is common knowledge that the immediate management and treatment of the acutely ill patient has been altered. Large groups of chronic patients heretofore secluded in the continuous treatment wards of the hospital have been mobilized, and new categories of patients, with special needs of their own, may well be emerging. Also, such rehabilitative measures as have been empirically achieved have increased and made more urgent the contacts between the mental hospital and the community. Accurate figures in all these respects, however, are not readily available at present. Nor has the impact of the new therapies on staff attitudes and staff skills and on the emergence of novel responsibilities for ward personnel been systematically assessed. In conjunction with the Laboratory of Socio-Environmental Studies, the Psychological Laboratory, and the Biometrics Branch of NIMH, it is hoped to give early thought to the design of a series of documents aimed at answering certain specific questions relating to these various areas: to test and recalculate these in different therapeutic settings of the hospital; and, in the light of experience, adopt some documents which would with reasonable accuracy measure subjective and objective change in the patient and the environment within which he functions. It is hoped to reduce these data to a statistically manageable form, and to apply them to wider populations than the one for which they were originally intended.

The design of the above documents will proceed pari passu with the design and calibration of documents used in a study of the placebo response, and the systematic trial of new agents. It is hoped that these studies will be conducted in conjunction with the Psychopharmacology Service Center.

A further function of the Section will be to determine and classify the mental and somatic responses to established and new drugs in relation to the nature of the individual illness, the phases and the changing patterns of the course of an illness and the genetic background of the individual patient. Relatively little is known of the relation of drug reactivity patterns, in either mental or metabolic
terms, to genetic factors. It is intended to single out a few selected syndromes, such as the depressive syndrome, certain phasic mental disorders, and stable schizophrenic states, for intensive clinical, psychophysiological and metabolic studies. These will be conducted in a metabolic ward and will aim at establishing correlates between clinical, somatic, biochemical and endocrine responses to graded doses of individual drugs and metabolites; and by the use of suitable techniques (including animal techniques - see below) at defining the relationship between biochemical events in tissue fluids, and intra-cerebral events. The interplay between the nervous, and the endocrine systems may be particularly relevant in this context; and may perhaps, in time, contribute to a definition of prognostic indicators in the choice of individual drugs for particular syndromes. Furthermore, it is hoped that drugs discriminatingly used may lead to the recognition of pharmacological and biochemical cleavage planes between syndromes bearing a superficial clinical resemblance; and thus contribute to a clearer classification of the phenomena of mental disorder than has been possible on clinical grounds alone.

2. **SECTION OF CHEMICAL PHARMACOLOGY**

The activities of the Section will be closely related to both the functions of the Section of Psychiatry and the Section of Behavioral Sciences. In the clinical field, this Section will be responsible for the conduct of human studies in intermediate metabolism, and the establishment of the biochemical correlates of drug reactivity patterns in the individual patient. Also, using tracer techniques, an attempt will be made at a clearer recognition of the relationship of systemic biochemical events to events within the central nervous system. The precise metabolic pathways affected by selected drug, and the metabolic fate of drugs will also be studied.

In the experimental field it is intended to carry further the examination of the effects of drugs on enzymatic processes concerned in the synthesis, storage and release of neurohumoral agents within the brain, with special reference to the possible existence of three types of drug receptors related, respectively to a naturally occurring choline ester, catecholamine, and indole. It is hoped that attention will be directed toward the effect of drugs on the operation of hormonal mechanisms, within and outside the central nervous system, with special reference to pituitary function; and, at a more cellular level, to an examination of drug effects on carbohydrate and nucleotide metabolism in the central nervous system. The fluorimetric and tracer methods used in these studies will be intimately related to parallel pharmalogical and electrophysiological studies in the Section of Behavioral Sciences.
3. SECTION OF BEHAVIORAL SCIENCES

The work of the Section of Behavioral Sciences will be closely related to the work of the other Sections, and also to some studies currently in progress in the laboratories of Clinical Science and Psychology at the Clinical Center. In the human psychological studies, particular attention will be paid to the processes of attention, 'set', sensory discrimination, and learning in the schizophrenic and depressed patient in various phases of illness, and the effects of drugs upon these processes. An attempt will also be made to establish objective measures for those aspects of thought disorder which are characteristic of the schizophrenic syndrome, and which are measurably affected by drugs. Somatic measures will center on various aspects of autonomic and fine motor function, and the spontaneous and induced electrical activity of the brain.

These studies will be linked to studies of the effect of drugs on the function of sensory pathways in the experimental animal, with special reference to the coding and transformation of information along various levels of integration within a sensory pathway. Microelectrode techniques will be used in these studies, and an attempt will be made to link concepts of modern information theory to data obtained in physiological and pharmacological experiment. The operation of highly patterned inhibitory fields operating within the central nervous system may be relevant in this context. The capacity of the brain as an information-storing, matching and predicting organ is disturbed in certain stress states, in drug induced states, and in schizophrenia. These disturbances may have their chemical corollaries. It may, therefore, be appropriate to carry out these studies in a hospital setting where clinical disturbances in the handling of sensory information, though not uncommon, have not so far received the experimental scrutiny they merit.

A further aspect which it is hoped to pursue in this Section is the systematic study of the electrophysiological equivalents of learning in the normal animal, and in animals subjected to either anatomical or biochemical lesion. Techniques in this regard, though still at an early stage of development, promise well, and may gain by being linked to the techniques used in the studies in the sensory physiology field.
LABORATORY OF CLINICAL SCIENCE
Seymour S. Kety

The area of interest of the Laboratory of Clinical Science lies in the application of the biological sciences to the problem of mental disease. The individual sections of which the laboratory is composed, representative of the various biological disciplines, work freely within this broad field concentrating upon certain clinical or basic studies which they pursue independently or in collaboration with each other or with other laboratories and institutes. In July of this year a second ward was placed under the direction of this laboratory, making possible the initiation of a long-range multidisciplinary program of studies in the biological aspects of schizophrenia. Since this is expected to be the central program of the laboratory for the next several years, some discussion of its historical background and methodological approach seems warranted.

Biological Aspects of Schizophrenia

There is a long history of theories and findings which postulate or purport to demonstrate characteristic biological changes which operate at a fundamental level in this important field of neuropathology, where definite pathological change in the brains of schizophrenics was reported by Alzheimer in 1897 and by Mott in 1920. More carefully controlled studies by Dunlap in 1924 and Conn, ten years later, failed to reveal significant changes from the normal, so that at the present time there is no pathological change generally accepted as characteristic of this disease. More cogent has been the evidence acquired by studies of its genetic aspects. Studies by Kallmann of a large population of schizophrenics had shown a high incidence of mental illness in their immediate families, an incidence which increased progressively with consanguinity, making it compatible with but by no means proof of the genetic factor. Studies on uniovular and biovular twins by Luxemberger in 1928, Rosanoff in 1934, Kallmann in 1946, and more recently, Slater in 1953 have shown a concordance rate in the uniovular twins varying from 60 to 86 percent, with a concordance rate in the biovular twins identical with that in siblings, which is about 10 to 14 per cent. Although none of these studies is free of important methodological defects which would tend to exaggerate the concordance rate in uniovular twins, the close agreement in the concordance rates by several investigators using somewhat different approaches and studying patients in different countries strongly suggests an important genetic element in at least a large fraction of schizophrenics.
In the field of electrophysiology, as early as 1941 Finley reported a higher incidence of electroencephalographic abnormalities in schizophrenia (28 per cent as compared with 7 per cent in normals). A series of reliable investigators have confirmed this high incidence with frequencies ranging from 23 to 60 per cent in this disease. These findings are compatible with the reports by Heath and by Sem-Jacobsen of paroxysmal spiking activity in deeper cerebral structures in a large percentage of schizophrenics. The electroencephalographic evidence has formed the basis for the current project by Evarts, McDonald, Pollin, Snyder, and Butler on behavioral and biochemical correlates of the electroencephalogram in schizophrenia, where preliminary studies have revealed at least one positive correlation with biochemical changes in the blood.

Although there has been some emphasis on the endocrinologic changes in schizophrenia in the past, there is little confirmed evidence of endocrine disturbance in this disease which cannot readily be explained as being secondary to the anxiety and stress which characterize this condition. The same comment is true of circulatory changes. In his current project in this area, Cardon has found little cardiovascular deviation except for a diminished ballistocardiogram.

There has been much speculation concerning disturbances in the circulation and energetics of the brain in schizophrenia. The Section on Cerebral Metabolism and the Section on Psychiatry have confirmed and extended previous work in this field in showing that although there may be a correlation between certain mental states and cerebral oxygen consumption, there is no abnormality either in circulation or total oxygen consumption of the brain in schizophrenia.

Much of the biological work and many of the findings have been in the field of biochemistry as related to schizophrenia. There is some agreement in the literature of some disturbance in carbohydrate metabolism, i.e. a reduced glucose tolerance and an increased insulin tolerance, although to what extent this is primary is in doubt.

Many of the biochemical studies in the recent past have concentrated on various aspects of protein and amino acid metabolism. Gjessing in Norway first showed a correlation between nitrogen balance and the mental changes of periodic catatonia. More recently, there have been reports of altered excretion patterns of amino acid and phenolic amines in schizophrenia by Williams and by McGeer and their respective associates, findings which have not generally been confirmed. One major program of the laboratory is a systematic examination of the metabolism of certain amino acids (e.g. phenylalanine, tyrosine, tryptophane, histidine, glutamine) in normal man and in patients suffering from schizophrenia.
There are at the present time three hypotheses, widely held, if poorly supported, for a significant biochemical mechanism in the pathogenesis of schizophrenia. These involve, respectively, epinephrine, ceruloplasmin, and serotonin. The epinephrine hypothesis postulates a disordered metabolism of this hormone in schizophrenia with the production of toxic schizophrenogenic substances. It is based upon the unconfirmed finding of Osmond, Smythies, and Hoffer of hallucinogenic properties in adrenochrome and adrenolutin, and on the finding by Leach and Heath of a more rapid oxidation of adrenaline in vitro by schizophrenic serum. McDonald and the Section on Medicine have confirmed the latter finding but have shown further that it is related to and probably explained by the low levels of ascorbic acid usually found in unselected schizophrenics. Since there is no evidence for the formation of adrenochrome or adrenolutin in vivo in normal or schizophrenic man, a project is under way in the laboratory which is studying the effects and fate of this important hormone in these two populations.

An elevation in the copper-containing globulin, ceruloplasmin, in the serum of schizophrenics was first reported in 1955 by Ozek in Germany, and in 1956, Leach and Heath demonstrated that it was the important enzyme in the in vitro oxidation of epinephrine. In 1957 Akerfeldt, in Sweden, applied the dimethyl-paraphenylenediamine test for ceruloplasmin to schizophrenic serum and showed that the positive reaction was related both to an increased ceruloplasmin and a decreased ascorbic acid. In the past year, McDonald and his associates in the Section on Medicine have shown further that ceruloplasmin is not characteristically high in schizophrenia, and that the positive Akerfeldt test in this disease is more the result of a low ascorbic acid which is probably on a dietary basis, since he was able to demonstrate normal levels of this vitamin and a negative Akerfeldt test in schizophrenic patients at the Clinical Center kept on an adequate normal diet. This interest in ceruloplasmin has prompted the initiation of a project by Hansen in the Section on Cerebral Metabolism on copper metabolism in normals and schizophrenics. An outgrowth of the ceruloplasmin hypothesis has been the reported isolation by the group under Heath of a substance, taraxein, reported to be an altered form of ceruloplasmin which they find capable of producing certain of the manifestations of schizophrenia on injection into prisoner volunteers. Robbins and Smith, on the other hand, have been unable to confirm these findings. The laboratory awaits better characterization of this substance and more reproducible techniques for its production before attempting to evaluate these reports. Interest has also been aroused in the laboratory by the preliminary report of Winters of the ability of small doses of schizophrenic serum to produce behavioral changes in the rat. A discussion has been arranged with Winters for the purpose of working out some collaborative validation of these findings.
The hypothesis that an abnormality in the metabolism of serotonin occurs in schizophrenia stems from the discovery by Hofmann in 1943 of the hallucinogenic properties of lysergic acid diethylamide and the demonstration by Gaddum and Woolley, independently, of an antagonism between this substance and serotonin. Further support has been found in the demonstration by Udenfriend, of the National Heart Institute, of the presence of enzymes for the formation and destruction of serotonin in various parts of the brain, the isolation by Horning of the National Heart Institute of dimethyl-serotonin from the cohaba bean, and the demonstration by Isbell, of the NIMH Addiction Research Center, that dimethyl-serotonin possesses hallucinogenic properties. This hypothesis is compatible with findings of Brodie's group in the National Heart Institute of a release of brain serotonin on the administration of reserpine and the behavioral effects reported in animals and man of the administration of marsalid which increases the brain serotonin content. The only evidence at hand, however, for an actual disturbance in serotonin metabolism in schizophrenics is the finding by Zeller that such patients fail to show the normal increase in 5-hydroxyindoleacetic acid which he has found to follow the administration of tryptophane. Several projects contemplated or initiated as part of the amino acid metabolism program of the laboratory propose to test the metabolism of tryptophane and serotonin in schizophrenic patients.

Even a casual review of the literature reveals no dearth of positive findings in schizophrenia from every biological discipline. On the other hand, it is extremely difficult to find any which have been confirmed by others or for which there is evidence that they are characteristic of a significant proportion of schizophrenics and fundamental to the process rather than being completely secondary to the disease or to present methods of its treatment. There appear to be at least two factors operating to produce this unfortunate state of affairs, in addition to the emotional domination and tendency to report preliminary results quickly and widely which seem to characterize research in those diseases which constitute important national problems. The diagnosis of schizophrenia, being entirely phenomenological and clinical and without etiological bases, is apt to include a number of different diseases with a common symptomatology. This would introduce major sampling errors in studies on relatively small samples, especially those limited to a population at a single institution as practically all of these studies have been, and might help to explain the extremely large variability in biological data obtained on "schizophrenics" and the infrequency with which these are confirmed by subsequent investigators. Perhaps a more important factor has been the general failure to control the important non-disease variables, which are either secondary symptomatic features of the disease or which are associated with the chronic hospitalization to which most of the patients are subjected. The "controls" for most of the studies in schizophrenia have been hospital or laboratory staff under normal conditions of life.
We feel, nevertheless, that this is a particularly propitious time for a major effort in this field, hopefully avoiding or, at least, attempting to minimize some of the methodological pitfalls to which previous studies have been subject. The recent twin studies of Kallmann and Slater, confirming and extending those of previous workers, strongly suggest an important role for biological factors in the etiology of many types of schizophrenia. In the past two decades the field of intermediary metabolism has been largely written and a wealth of basic information made available on possible biochemical mechanisms which have been studied only partially in normal man and practically not at all in schizophrenia. There are, furthermore, certain new techniques which were not available to previous studies: chromatography for the separation of large numbers of constituents, various techniques of spectrophotometry utilizing ultraviolet, infrared, or fluorescence for the sensitive detection and quantification of chemical substances, and the use of isotopic techniques for the tracing of metabolic pathways in man.

Dr. Perlin and the Section on Psychiatry has given considerable attention to the problem of selection of patients, in an effort to minimize the incidental and non-disease variables in the sample and to maximize within the sample the incidence of those forms of the disease in which genetics and biological factors operate significantly. These patients are housed in the Clinical Center and maintained under optimal dietary and therapeutic care in conditions which tend to provide a normal amount of activity, and with appropriate psychotherapy designed to minimize the disturbance and the anxiety associated with the institutionalization and with the observations themselves. The schizophrenic group is controlled by means of a population of normal individuals, maintained as much as possible under similar conditions of diet, activity, and management.

These two controlled populations offer to the members of the laboratory and to other interested investigators a unique opportunity to test various hypotheses relating to schizophrenia and to correlate their findings with those of others in different fields who have studied the same population. Reference has already been made to some of the specific projects now under way or being initiated which include studies on electroencephalographic changes, the effects and fate of epinephrine, blood levels and metabolism of glutathione, copper, ceruloplasmin, and ascorbic acid, and the metabolism of such amino acids as tryptophane, histidine, glutamine, and tyrosine.
RESEARCH OF THE SECTIONS

The Section on Psychiatry under Seymour Perlin has concerned itself with psychiatric variables and their correlations with biological measurements. In the past year an interesting relationship has been discovered between cerebral oxygen utilization and certain personality traits or the psychological state of the individual at the time of the procedure. These studies are being extended to determine whether the relationship is maintained. A careful psychiatric study by Pollin and Perlin of normal volunteers has elucidated a very high incidence of significant psychopathology which was highly and inversely correlated with the extent to which external factors operated in the volunteering process. This represents a contribution of considerable significance in clinical investigation on volunteer populations. Reference has already been made to the excellent theoretical study and practical achievement in the problem of selection of an adequate population for biological research in schizophrenia.

The Section on Physiology under Edward Evarts has continued its program of studies related to the correlations between drug action, behavior, and electrophysiology. By means of chronically implanted electrodes in trained, conscious animals, clear-cut differences between the cortical effects of hypnotic and atarctic drugs have been demonstrated. The absence of cortical depression by the latter group may help to explain the selective behavioral effects of these drugs. Clinical psychological studies by Kornetsky on a number of centrally acting drugs have revealed significant effects on intellectual, motor, and perceptual skills by meperbamate in normal subjects. In schizophrenic patients single therapeutic doses of chlorpromazine or secobarbital produced similar impairment of intellectual, motor, and perceptual functioning, but during chronic administration of these agents, the deficits associated with chlorpromazine disappeared.

One of the major interests of the Section on Medicine, headed by Roger McDonald, has been the interrelationship between the nervous and endocrine systems as indicated by the hypothalamo-hypophysial system. In the past year McDonald has evaluated a widely held concept that pitressin is the neurohormone which directly stimulates ACTH release from the anterior pituitary gland. In a series of crucial experiments he has shown that pitressin and ACTH release can occur independently of each other and that morphine, which acts on the central nervous system, effectively blocks the ACTH release associated with pitressin, thus demonstrating that the pitressin effect is not a direct one upon the anterior pituitary gland. The studies of McDonald and this section on many of the biochemical disturbances thought to be associated with schizophrenia, highlighting nutritional factors as their probable cause, have already been mentioned. They have brought a new and critical approach to the field of the biology of schizophrenia, an approach much needed lest this important interest be stifled in its very reawakening by overenthusiastic and undercritical conclusions.
Laboratory of Psychology
Dr. David Shakow

As has been pointed out in previous annual reports, the program of the Laboratory, despite having certain clear-cut areas of activity such as is represented by the separate Sections, is best viewed as a whole and in mutual context. I shall therefore combine the report on the activities of the seven Sections which comprise the Laboratory without making a distinction as to source of support -- Clinical Investigations or Basic Research. I shall concern myself first with reports on the status of various studies and then consider other material of relevance as an annual report.

Although there are still four important programs which have not reached the stage where they may be considered as actually launched, the rest of the work of Laboratory in this fourth year of activity is well under way. This, despite the fact that two Section Chiefs, those in Personality, and in Learning and Perception, have not as yet been appointed. It appears, however, that the first problem will be solved as of the middle of next year, and various plans are afoot to solve the second. In the meantime, the Acting Chiefs of the two sections have worked most conscientiously at their tasks of keeping the administrative machinery going.

Although some work has already started, the major program in relation to schizophrenia is still to be worked out. With respect to the research to be carried out on wards 3-W and 3-E some preliminary planning is in progress but largely it awaits the coming of the new Chief of the Adult Psychiatry Branch. We are most anxiously awaiting this development since it will afford us an opportunity to deal with more molar and social aspects of schizophrenia -- a necessary complement to other kinds of schizophrenia research we are carrying on and planning. Since this summer we have been carrying out a series of studies on wards 4-W and 2-W, but these have been considered largely pilot projects to develop methodology and refine our concepts. The principles for the selection of patients and controls on these wards having been established, we are now ready to enter with a more definitive program. The schizophrenia program to be carried out at St. Elizabeths Hospital is in part awaiting the completion of the construction which is going on there at the present time and the period of basic relation-building which Dr. Elkes is now in process of carrying out in this new set-up. By the beginning of the next year it is hoped that a program of research utilizing this unusual facility will have been formulated.
Although minor sub-projects have been carried out, the central Psychotherapy Sound-Movie Program has suffered serious delays over a three-year period because of the slowness with which construction of both the room and projector equipment has proceeded. However, it looks as if the major construction work will shortly be over and with the coming of Dr. Bergman plans have already been laid for actually carrying through a full psychoanalytic psychotherapy. The problem of freeing more time for this study for the two major investigators now becomes acute.

In presenting the present programs, I plan in general to follow the organization of last year's report; that is, to present the work of the various sections separately in order that the stage of development they have reached and what they are engaged in will be clear. It is important, however, that the section reports should be presented in the context of the general program of the Laboratory because there is a certain kind of artificial separation which derives from the section organization.

The general goal of the Laboratory, stated in its broadest terms, is the study of psychological function - both normal and pathological - in the context of specific behaviors or in more generalized structures of personality. In many instances these functions are studied explicitly in relation to nervous and other somatic systems. In other instances they are studied independently and with only an implicit acceptance of such relationships, either because these relationships are not immediately relevant, or are not presently available for study. This broad but focal concern with psychological function is approached through various avenues, each of which contributes to the total picture. These approaches may be roughly designated as the study of the developmental, aging, mature, and pathological aspects of the organism. The last is considered both with respect to the character of the pathology and with respect to efforts at its modification, whether through individual psychological, psychosocial or physiological means.

Against this background I shall first consider the work of the three sections of the Laboratory in the Clinical Investigations area: Child Development, Personality, and Section of the Chief.
Child Development

The Section on Child Development has continued its researches along the general pattern set in previous years, an emphasis on the study of basic processes and developmental aspects of behavior in infants and young children. Several studies have been carried through to completion, and new ones have been initiated. The five senior members of the staff all continue in the program. One psychologist at the Ph.D. level, Dr. Yvonne Brackbill, was added to the staff in August, to assist Dr. Gewirtz with his studies on infant learning. Dr. Belinda Straight, as a guest investigator, has continued cooperative work with Dr. Bell in the study of one-month old infants and their mothers.

Research in the section is directed toward evaluating the inherent, maturational and environmental determiners of personality and development in infancy and the persistence of early emotional and behavior patterns, as they relate to mental health. At present several fundamental methodological and procedural studies are under way. Some of these studies are concerned with devising tools for use in a more general longitudinal study of personality development. The children selected for study are presumably normal, although some selections of subjects are made on the basis of specific conditions that could affect mental health. For example, in addition to babies in normal homes, we are studying infants living in institutions and infants whose parents have contrasting and possibly psychopathogenic personalities or attitudes toward child rearing practices. One group of studies is concerned with available data from the Berkeley Growth Study, in which characteristics of the mothers' personality are related to the personality and development of the children (on whom records are available from birth to 18 or 25 years). Significant relations from this study are utilized in devising tests and procedures for further studies of infant development.

The researches of Dr. Gewirtz are concerned with the etiology and conditions of dependency and attention-getting behavior, an area of importance because it is an aspect of the central problem of how social learning takes place. Working with nursery school children he has experimentally observed this behavior under conditions of social reinforcers (approval), and their effect in situations of satiation and deprivation, and has demonstrated significant relationships. (1) Brief social isolation (equated to a condition of deprivation of all social reinforcers) increased reliably the reinforcing power (i.e., the importance) of adult approval for children (aged 4-0 to 5-6) as a positive function of the degree to which they typically
sought such approval in other settings; and older children in this age range were affected to a greater extent than were younger children. (2) In children aged 6-6 to 9-0, it was found that brief social isolation (deprivation) enhanced the effectiveness of social reinforcers representing approval and social contact relative to a control condition (no treatment); and that a brief condition of satiation for approval and social contact decreased the effectiveness of those social reinforcers relative to the control condition. Dr. Gewirtz's current program, with Dr. Brackbill, is directed toward observations of infants under one year of age.

Methods are being explored with very young children which reduce to relatively simple terms the complexities of the behavior which characterize emotional dependence in later childhood and which would relate those behaviors to critical aspects of myriad environmental conditions to which young children are typically subject. A series of prototype experiments with human infants in a highly controlled institutional setting represents the core of the experimental program. Initially, these experiments will attempt to relate effects in the child's pattern of emotional dependence to variations in selected aspects of the caretaking process. At first, the reinforcing aspects of caretaking and adult responsiveness to the child are employed as variables; and the range of adult responses which can function as reinforcers for the young child's behavior will be explored. Selected stimulus events associated with the caretaker are being set into a variety of contingencies with different responses emitted by the child. After some of the more common reinforcers which are provided by adult responses are determined, selected stimulus events (e.g., the attention of a caretaker) involved in or attached to the caretaking person may be set into a variety of contingencies with these reinforcing aspects of the caretaking process; and selected aspects of this process may be made contingent upon different responses emitted by the child.

Dr. Rheingold is carrying out a series of studies on social responsiveness in infants. Her work has been with children in institutions, with re-tests in their homes of children originally observed in institutions, and with comparisons between behavior in their homes and in a strange place of the same children. In a monograph now published, she demonstrated increasing social responsiveness in institutional babies who were given individualized maternal care, and she (together with Dr. Gewirtz) has just completed a study in which she was able to increase vocalizations in three-month old babies by positive social reinforcement.
In a pilot study of a few infants living in their own homes, Dr. Rheingold has tested the developmental changes in social responsiveness to known persons and to strangers, and compared the difference of the infants' behavior in their own homes and in a strange testing room. She has found evidence of significant differences and plans to extend these studies to a larger population. Data are now being analyzed of observations made by Dr. Rheingold and Dr. Bayley who re-visited at 21 months of age infants first studied at 6 months while living in an institution. Half of these infants had had an 8-weeks experience of special care-taking by a single person. The follow-up study was carried out to look for any evidences of long-term effects of the specialized care. Some slight differences of manner of social responsiveness are suggested.

Dr. Bell is conducting studies of early phases of mother-child interactions on samples selected on the basis of the mother's expressed attitudes toward children and child-rearing (the PARI). Motion picture records of the infants are made of standardized situations at 3 days of age, and of the mother-child pairs at one month of age. Ratings of the mothers' behavior are being compared with their responses on the Parental Attitude Research Instrument; the characteristics of the infants are being rated at three days and at one month of age. Consistency of the infants' behaviors, as well as patterns of mother-child interaction relevant to the maternal attitudes are being studied. The data having been collected, they are now in process of analysis by a variety of methods. The general approach used appears to have provided quite rich data on the nature of the early child-mother relationship.

In addition to the PARI, a questionnaire-rating scale filled out by the mother to express her attitudes to child-rearing (described in earlier annual reports -- which, by the way, has received extensive use over the country), Drs. Schaefer, Bell and Bayley have prepared for publication two Maternal Behavior Research Instruments, which were developed for quantifying descriptive material from the case files of the Berkeley Growth Study. One of these instruments is based on material derived from interviews with the mother about child-rearing and development which is carried out by a sophisticated child clinician; the other is based on direct observations of child-mother interactions in a relatively standard situation. Dr. Schaefer has utilized this and other material in applying factor analyses and Guttman's radex methods to the intercorrelations of maternal behavior scores, and has concerned himself with developing, around the resulting pattern of maternal traits, a theory of certain aspects of personality
organization: the two factors of autonomy-control, and love-hostility form the frame in which the traits are organized in a circumplex.

Drs. Bayley and Schaefer are carrying on a series of studies of the Berkeley Growth Study material in which the maternal personality scores are being correlated with other parental data and with the children's scores. Findings so far show patterns of relationship of maternal traits to socio-economic status, to children's happiness and activity and to children's intelligence scores, which if corroborated by further study would have important implication for child-rearing.

A few of the findings might be mentioned here: Correlations between the maternal traits and socio-economic status show the higher status mothers to grant more autonomy to their children, to be more cooperative in the testing situation, and more equalitarian in their interactions with their children. Lower-status mothers tend, on the other hand to maintain close contact with and to be more intrusive, irritable, punitive and ignoring of their children. When compared with characteristics of the children, those children whose mothers grant autonomy are equalitarian and cooperating, express affection, tend to have below-average intelligence scores as infants but to earn increasingly higher "IQs" to about six years and remain high through 18 years. In contrast, those children whose mothers are punitive, irritable and ignoring tend to have high scores as infants but to develop slowly with even lower "IQs" to about 6 years, after which age they remain low. In both of the above sets of comparisons the relations are much stronger for the mothers of boys, than the mothers of girls. Among personality ratings of the children, cooperative, equalitarian, affectionate mothers tend to have babies who are happy, calm (unexcitable) and "positive", while the irritable, punitive mothers tend to have infants who are rated as more active. The same relations tend to hold for the boys after they are as old as 8 years, in ratings related to their socially responsive, cooperative and intellectually efficient behavior; in these variables the boys who score high tend to have cooperative, equalitarian, affectionate mothers who had close contact with their babies. The boys who rated low more often had mothers who were punitive, irritable and ignoring. Further study is necessary to clarify the nature of these relationships.

As part of a program for studying development in infancy, Drs. Bayley and Schaefer have been trying out on infants and successively revising, methods of recording and rating both maternal and infant behavior observed during the infant development tests. In connection with this program Dr. Bayley is
preparing her California First Year Mental Scale, for a thorough revision and restandardization. This revision is being undertaken as a necessary preliminary to the infant study because currently available tests for infants are out of date, inadequately standardized and procedures and scoring poorly defined. It is planned to correct these inadequacies and to expand the test to include emotional and attitudinal scores that will permit a more comprehensive evaluation of the infant as observed in the test situation.

Theories of the early formation of personality, both of emotional adjustment and intellectual development are based on rather general studies with very little experimental work under specifically controlled conditions. The primary research efforts of this section are directed on the one hand toward identifying more or less specific environmental conditions that can influence the course of development, and on the other hand toward studying in infants their developing capacities to learn, and the stability of both learned (or conditioned) behaviors and of maturational trends in response tendencies. Once these are better understood it will be possible to state more explicitly the determining factors in the dynamics of personality formation.

The personnel and program of the section are utilizing to the fullest extent the facilities available to it. It is at present necessary (both for lack of facilities and by demands of the research designs) to make a large proportion of the observations in facilities outside of the NIMH, in hospitals, well-baby clinics, orphanages, and in the infants' own homes. For certain of the studies it would be desirable to have accommodations either in the Clinical Center or in a separate building, for housing normal, healthy infants who could be made available for continuous study over periods of a few days to several months, and either with their mothers or on a "Foster care" basis. It is hoped that such a facility with the augmented staff and caretaking personnel it would entail will be considered seriously as an important aid to the Child Development research program.

**Personality Section**

The program outlined in previous annual reports of this Section has necessarily undergone some modification with the resignation of two of the four investigators of the Section. The remaining two investigators have continued their studies of the process of change in attitudes, value systems and personality. The central focus of the Section continues to be the development, testing and extension of current personality theory. More specifically, the major effort of this Section is
the application of personality and social influence theory to the problems of modification of attitudes, value systems and behavior.

The ward milieu studies dealing with preferred nursing roles have been completed this year. In line with the developing program on ward 3-W studies will be undertaken to analyze the nature of relationships existing among the hospitalized schizophrenic and his parents. Although investigation of psychosomatic disease came to a temporary halt with the resignation of Dr. Iflund, it is planned that some studies in this area will be continued by Dr. Handlon.

In planning the future directions of the Section, an effort has been made to select personnel who will be able to work closely with the Adult Psychiatry Branch in research and case evaluation. Drs. Handlon and Waldman, who came on duty in September, give promise of fulfilling this goal. They are already actively engaged in planning collaborative research programs with psychiatrists, sociologists and members of other disciplines active on the Adult Psychiatry and Clinical Sciences wards.

In the ward milieu studies we have to date been concerned with one important aspect of ward milieu, namely, the nursing role as it relates to the treatment of schizophrenia. In this setting efforts have been made to introduce predetermined ward philosophies on the experimental basis. Under these conditions, it is necessary for the experimenter (the ward administrator) to communicate his concepts to the nursing staff and to help them accept and apply them in order that the desired experimental condition be achieved. The problems inherent in this mode of research have offered a very practical and real-life situation in which to investigate conditions affecting attitude change. Over a period of two years data have been gathered concerning the impact of five unique ward philosophies on the psychiatrists and nursing personnel. It has been found that psychiatrists and nurses show consistently different concepts of the preferred psychiatric nursing role and this offers a basic problem for collaboration. It was further noted that although nurses may show attempts at modification of their nursing concepts in the direction of the new ward philosophy, these changes are unstable and disappear over time. It was concluded that the less acceptable a ward administrator's philosophy was to nurses initially, the less it was finally accepted by them even after as much as 21 months of exposure to it. These studies have not as yet been extended to measuring the effect of a given ward milieu on patients inasmuch as the desired ward atmospheres, i.e., the
experimental conditions have not been achieved. Other studies of the development of psychiatric nursing attitudes were undertaken with nurse trainees, graduate nurses and experienced psychiatric nurses. It is clear that with the greater crystallization of the nurse's identity as a professional individual, her amenability to roles quite deviant from her own preferred nursing role becomes progressively reduced.

It is anticipated that this Section will become increasingly involved with ward studies particularly as the contemplated studies of patient-family interactions get under way. Efforts will be made to investigate the premorbid and postmorbid patterns of interpersonal communication unique to families having a schizophrenic member. It is planned that carefully controlled studies will be made using a variety of techniques including the quasi-groups technique where unknown to the subjects, the process and substance of interpersonal communication can be systematically manipulated.

Two major investigations have been conducted in the area of psychotherapy. One involves research regarding moment-to-moment changes in the ego organizations of patients in the course of psychotherapy. Current work is mainly concerned with the investigation of a speech disruption measure adapted from Mahl in its relation to these ego states. Currently attempts are being made to determine the influence of rate of speech on the incidence of such speech disruptions. The continuing aim of this investigation is to use these and other measure to define shifts in a patient's ego state. The second investigation in the area of psychotherapy relates to the communication of therapist's values and preferences for types of content and emotional expression in the course of therapy. This was investigated in the treatment of two schizophrenic patients. This particular study was completed in its writing stage this year. It has, however, given impetus to a broader program of study. It is planned that some of the implications regarding values and expectations of patient-therapist pairs will be the basis of a program of research regarding "drop-outs" from therapy. It is becoming increasingly evident that a sizeable proportion of the total number of patients referred for psychotherapy drop out of treatment without benefit during the initial phases of therapy. These patients are described in sociological terms as coming predominantly from the lower socio-economic groups. It is hypothesized that with further analysis of these individuals, it will be found that an important variable affecting drop-out rate is the nature and degree of discrepancy between therapist's and patient's values and role expectations. It is proposed that a study of the psychological variables resulting in such communication failures will be investigated. The next step of the proposed program would be the
utilization of the identified variables in treatment and in quasi-treatment groups in order to facilitate communication and the adaptation of the psychotherapy situation to the special needs of this large group of patients. Such a program would have both theoretical and practical significance.

Another aspect of the "values" studies is a two year study regarding the communication of "moral" values in the course of psychoanalytic treatment which is being brought to a close. This may provide data related to the question of whether the intensive analytic relationship affects the moral values of a patient in the direction of those held by the therapist. An analysis of the pattern of change in moral values of each of the four patients studied will be undertaken.

Dr. Handlon plans to investigate the relationships among physiological states, individual personality structure and susceptibility to the various psychosomatic diseases in a program tentatively planned with Dr. Hamburg.

To date there have been but few attempts to develop instruments that permit the simple and economic assessment of the mental health of large segments of the population. Dr. Handlon is collaborating with members of the Socio-environmental Laboratory in the attempt to apply the Guttman Scalogram technique to the development of valid and reliable measures of "mental health".

The Section is also occupied with a research project which may perhaps be classified most appropriately as "service research", but which carries much wider implications. This involves the evaluation of the NIH Research Associates Training Program. The project touches on a very basic administrative question: How best to facilitate optimal interaction between the inherent capacities of the investigator and the stimuli provided by the setting to promote creative productivity. This project may develop into such scope that it may be necessary to bring in researchers on a contract basis or to assign investigators full time to this particular project.

Section of the Chief

The major areas of research in this section are schizophrenia, psychotherapy, and the psychological aspects of physical illness. In many respects the activities of this section overlap with those of the Section on Personality.
It is our expectation that when the Chief of the Personality Section is appointed, some reorganization of the two sections will take place looking towards further integration of the activities of the two groups.

At the present time the members of the section who are concerned with the problem of schizophrenia are Drs. Rosenthal and Zahn in addition to the Chief. One continuing study by Dr. Shakow involves the analysis of a large body of already existing experimental data on the psychology of schizophrenia as a basis for the development of theory in this field. During the year some progress was made on the analysis of this material. In part this was used for a paper presented at the Second International Congress of Psychiatry in Zurich. It is hoped that eventually this work will result in several monographs on the psychology of schizophrenia.

The major group of studies consists of four parts and will involve the members of this section who are working in schizophrenia as well as members of other sections working in this general area. It is essentially the over-all program in relation to Clinical Center wards and St. Elizabeths wards which is being planned as described in the introductory remarks to this report. Many of the studies will be carried out concurrently and collaboratively with other Laboratories of the Institute.

One series of studies deals with responsivity patterns in schizophrenics. For this Dr. Rosenthal has the major responsibility. Patients are being studied for their responses at both the autonomic and molar behavioral levels when confronted with a variety of orienting situations. This is in part an outgrowth of previous studies on reaction time and on response to other forms of simple stimulation which have indicated the existence of deficits in schizophrenic patients. For a preliminary study a group of 13 schizophrenic patients selected on the basis of alpha patterns have been under study since July 1957. The experiment is still in process but the analysis of the material should be begun shortly.

A second series of studies in which Dr. Shakow is particularly interested and which will be carried out with Drs. Rosenthal and Zahn might be terms "capacity" studies. A considerable variety of psychological functions have in previous studies been found to normalize themselves under conditions of either repetition or optimal conditions of cooperation. There are however some functions in which such a tendency towards normalization does not appear to exist at least in the
contexts in which they have been studied thus far. This persisting pathology appears particularly prominent in situations where speed of response is called for by the environment. It is the purpose of the planned series of studies to find out whether with repeated exposure to the same task over a long period of time and with the setting of optimal conditions for performance it is possible to achieve the same normalization as is found in the other group of psychological functions. Some preliminary studies have already been started in this area on our wards here but mainly they are awaiting the development of the wards at St. Elizabeths.

Still another group of studies, as yet not clearly delineated, involve affective situations where attitudes of acceptance or rejection by the environment enter prominently. These derive in many respects from studies carried out by Garmezy and Rodnick at Duke, dealing with patients having good or poor prognosis, and should help to make more understandable the incongruence between cognitive and affective functions as characteristic of this type of patient.

A fourth group of studies subsumed under this general program are the family and social studies now in process of planning to be carried out by members of the Section on Personality in association with the Adult Psychiatry Branch. (See Project No. M-P-P-(C)-9)

Dr. Rosenthal has carried the administrative responsibility for the general aspects of the scientific investigation of a group of identical quadruplet girls who have been under study by investigators from various laboratories for a period of several years. A large amount of data in different areas have been accumulated. The integration and evaluation of these data are to begin on a formal basis shortly. The psychological material is in process of analysis by Drs. Rosenthal, Parloff and Waldman at the present time.

The psychotherapy activities of the section center around Project No. M-D(C) 1, and as far as this section is concerned is being carried by Drs. Dittmann, Shakow and Bergman. Both methodological studies aimed at making the substantive attack on the problem easier and a systematic theoretical exposition of the area as a field for research are included.

During the year Dr. Dittmann has been involved in two major studies having to do with the micro-analysis of the complex data of non-verbal communication provided by the special technique of sound-movies which we are using. In one project Dr. Dittmann and
Dr. Lyman Wynne of the Adult Psychiatry Branch have attempted to find ways of coding speech in order to identify disturbances which may be used as an index of psychological disturbance. Pitch, stress, and juncture patterns were first studied with the conclusion that these microlinguistic phenomena were too closely related to the syntax of language to be carriers of emotional communication. The next attempt was to work with hesitations and breaks in speech. Although they could be coded with fairly high reliability these qualities did not seem to be related solely to anxiety, but to other, irrelevant factors. During the present year a third set of phenomena were worked with, the so-called "paralinguistic" phenomena. These include changes in duration, loudness, pitch, intensity, articulation, and vocalization as applied to unit of speech larger than the morpheme. Preliminary study indicates that these phenomena can be coded fairly rapidly and offer promise of eventual usefulness for dealing with one of the non-verbal communication channels.

Another study being carried out by Dr. Dittmann has to do with the judgment of facial expression from short sequences of motion picture film. A previous technique of showing short series of prints from motion pictures was abandoned as being too artificial. The present technique involves showing short sequences of film of about three seconds in length through a motion picture projector to the judges. Considerable reliability has been obtained across judges. A pilot study was run to test whether these scores could be related to other variables. Using sequences of film of a patient following either leading responses or confrontations by the therapist facial expressions showed greater relatedness and calm following leading responses and greater discomfort and apprehension following confrontations. Judgments based on speech with meaning filtered out and on content alone showed trends in the same direction. The technique appears to hold promise as a method of studying emotional communication as mediated by visual cues. Reliability on a very limited sample is high and the judgments can be related to other variables. If this method holds up it may give us a beginning towards the analysis of the visual communication channel.

During the last year Dr. Shakow did some additional preliminary work on the project dealing with the information to be derived from the repeated viewing of complex material. The purpose of the study was to determine what additional relevant information necessary for the understanding of various aspects of the therapeutic process could be derived from successive viewing of a film from a psychotherapy session and whether there were major differences in the additional information derived as between active and passive analytic approaches to the data.
Due to some limitations of apparatus and press of time much less than the desirable amount of study could be carried out. However, with the acquisition of our new projector it ought to be possible to carry this project out with greater facility. It is therefore being planned for the next year.

Another area of research is an psychological factors related to physical disease that is being carried out by Dr. Kendig in association with various of the other Institutes and with some outside agencies. Her major project is on the self-concept and body-image as related to disease susceptibility and organ choice. In this study she is exploring the attitudinal factors insofar as they affect health and longevity. She is particularly interested in early childhood attitudes which may be instrumental in determining the nature of the self-concept and the body-image, especially in relation to susceptibility to illness, organ choice, course and outcome of disease. At first Dr. Kendig used an extensive series of self-concept tests and a variety of projective techniques on a group of physically ill patients. However, these proved unsatisfactory since they seemed mainly to reflect the present self-concept and body-image as unfavorably modified by years of illness. It therefore seemed necessary for her to develop an elaborate detailed questionnaire or interview schedule which would disclose the attitudes towards the self and the body inculcated in early childhood, explicitly by direct instruction and implicitly by the emotional climate of the home and family reactions to illness. During the past year such an instrument has been devised and pre-tested on two patient groups and on one group of normal controls. The scales are now being drawn up so the data can be coded and treated quantitatively. In the course of the current year the expected coding of the interview schedule which has already passed through a number of forms will be completed and a weighted scoring system devised. It will then be used with groups of patients in five of the other Institutes and with normal control groups.

Partly in relation to this study and partly as an outgrowth of her association with the other Institutes at the Clinical Center Dr. Kendig has become involved in a study of intractable (phantom) pain with Dr. John Van Buren of NINDB and on precocious puberty and pseudo-hermaphroditism with Dr. Roy Hertz of the National Cancer Institute. Both of these studies throw light on the body-image and the self-concept and therefore contribute to her major project. She is also seeing a group of patients who are being studied for the effects of various drugs by Dr. Conan Kornetsky. Again in these patients she is interested in problems of body-image and self-concept.
There are a few other studies going on in the Section which are not directly related to these three major areas. One is a further development of the study which Dr. Dittmann has been carrying out with Dr. Wells Goodrich on interaction patterns of normal and hyperaggressive children, a project reported upon last year. Their work during the present year has been chiefly concerned with further reliability studies of the methods developed. In this connection Dr. Dittmann has undertaken a study of dimensionality of psychological variables using non-metric techniques. This is an attempt to deal with certain problems in ordering data derived from personality material.

Dr. Paul Bergman, who has recently arrived and who is to participate as therapist in the psychotherapy sound-movie project, will also undertake a program of research of his own. These are of course only in the planning stage at present. They are to be along the lines of the relation between the effects of psychosomimetic drugs and psychotherapy, and on the interaction of other adjuvants and psychotherapy.

In closing this summary of the work of the Laboratory of Psychology I should like to point up succinctly and without elaboration a few tentative but important generalizations which derive from the preparation of the reports of the several Sections. These refer to common trends which appear independently despite the diverse approaches to the study of psychological functions by different methods and with different subject matters.

The first of these is a methodological point -- that of the value of the comparative method. It is through the comparative approach that we become impressed with the tremendous potentialities which lie in the interaction of the complicated psyche of the human (and its associated nervous system) with a stimulative complex social environment. We get an inkling of what such an interaction does for the full development and exercise of the organism's capacities. This picture is made even more vivid when we see these same principles reflected in lesser degrees in lower orders of animals, in the aged, in psychoses, etc.

Thus, we see in the report of the Aging group evidences for the potentiality of the organism for maintaining a high level of psychological function despite some biological decline. The difference between younger and aged rats is in many respects small or even non-existent. Also, this time in human subjects, similar scores are obtained in a variety of functions when the aged come from active rather than from limited institutional environments.
In the report of the Section on Animal Behavior we find that even when the human organism is damaged physically in an important part of its brain, the potentiality for recovery is great. Thus after frontal lobe damage monkeys seem to be permanently affected in delayed-response type tests, chimpanzees are also impaired but are able to recover with retraining; in man there does not seem to be any consistent damaging effect on problem-solving behavior. We also see a similar phenomenon in studies we have made of schizophrenics where optimal environmental pressure frequently brings patients close to capacity levels which are not far from the normal. We find it at another level in Dr. Calhoun's report of the importance of social factors in space utilization by mice and shrews living in woodlands. And we may have similar data from Dr. Kendig's studies soon in still another area -- physical disease and organ choice as related to the self-concept and the body image.

All of these studies seem to be leading in the direction of saying that despite the genetic factors which may be playing a role in either normality or pathology, the human organism has a tremendous range of potentiality which neither psychosis, nor age, nor brain damage can more than partially stay in its course if a social environment is provided which is sufficiently rich and appropriate to make demands on its potentialities. It is in this context that our developmental studies in handicapped, normal and superior subjects (both animal and human) become so important, for it is there that we can ask ourselves the important question: What is the process by which these potentialities are most effectively built up for optimal use, for resistance to destroying factors, and for recovery from such destroying factors?
Laboratory of Socio-environmental Studies
Dr. Marian Radke Yarrow

The research goal of the Laboratory is the investigation of the ways in which social processes bear upon the production and course of psychic disturbances. Included with this goal is a wide range of research areas: the nature and distribution of mental illness and behavioral pathologies, social and cultural variations in defining and treating behavioral disturbances, social and cultural patterns influencing personality development, interpersonal processes within the family, and social processes in the treatment setting of the mental hospital. This range of interests is represented in the current projects of the Laboratory.

With the growing recognition of the importance of social aspects of illness and with the realization that relationships between social and medical or biological factors are more complicated than has been assumed, there has been an intensification of research interests and efforts in conceptual and methodological issues and in collaboration across disciplinary lines.

During 1957, the organization of the Laboratory has been completed with the staffing of the Section on Social Studies in Therapeutic Settings.

Social Studies in Therapeutic Settings

In recent years there has been an increasing recognition of the therapeutic significance of the mental patient's social environment. The mental hospital is more than simply an auxiliary setting within which therapy goes on; it is a relatively long-term and all-encompassing life experience which, by virtue of the special nature of mental illness, necessarily has therapeutic consequences. This fact has led to an interest in studies of interaction among patients and between patients and staff, social role definitions of patients and staff, lines of communication and patterns of decision-making in the hospital, values, norms, and behavior of administrators, physicians, nurses, attendants, and patients, and various other aspects of hospital structure which appear to have consequences for the course of mental illness.
In 1957, for the first time, the Clinical Investigations Branch undertook to support the operation of such studies through its budget. This decision was followed by a period of active recruitment of social scientists who were motivated and equipped to cope with the problems in this field. This has been accomplished successfully. Since five of the seven professionals (including one Visiting Scientist) have entered this Section within the past two or three months, the general section program is still in its early stages of development. Dr. Morris Rosenberg has recently assumed direction of this Section.

Active planning is currently under way for the collaborative research with other units of the Clinical Investigations Branch. Mr. Turk and Mr. Lefcowitz are currently developing plans for research designed to form an integral part of the Neuropharmacological Program at St. Elizabeths Hospital. Dr. Pearlin and Dr. Rosenberg are collaborating with members of the Adult Psychiatry Branch and the Laboratory of Psychology in the development of a research program in Ward 3-West of the Clinical Center. Dr. Wallin is currently working with the psychiatric group in Ward 3-East of the Clinical Center in the intensive study of families of schizophrenics and is using this information for the development of scales about parent-child relationships associated with the development of schizophrenia. Such collaborative undertakings, to which a large part of the staff time is likely to be devoted, are pursued in the faith that the pooling of skills and perspectives from different fields will provide fruitful insights and valuable data bearing on the therapeutic process.

Mr. Perry, in his work at the Clinical Center, has provided a detailed demonstration of how the objective positions of staff members in the ward structure influence their attitudes and behavior toward the patients. These studies are scheduled for completion this year.

During the past year Dr. Goffman has continued his intensive investigation of the social life of the mental hospital patient at St. Elizabeths Hospital. Using participant observation, unstructured interviews, and case record sampling, he has succeeded in specifying some of the therapeutic implications of the pattern of involuntary incarceration and stigmatization which characterizes life in the mental hospital.


Publications (Cont'd)


Streicher, E. Biochemical investigation of the aging nervous system. In press.
Publications (Cont'd)


Clinical Investigations

BUDGET SHEET

Estimated Obligations for FY 1958

Total: $461,389

Direct: $353,652

Reimbursements: $107,737

Project: Neuropharmacology Research Center
INTRODUCTION

States and Territories have been receiving Federal mental health grants-in-aid and technical assistance for ten years. A major objective has been to help them establish sound administrative organizations at State level and to provide a well-trained multidisciplinary staff for leadership. This was essential to bring more direction to the scattered and often ineffective efforts in community mental health programs and to insure continuity of program. As a result, most States and Territories now have a professional staff developing a program aimed at public education, prevention, treatment, and rehabilitation. An increasing amount of training and research is being built into these programs.

The recent broad-based legislation for State grants-in-aid to localities for community mental health services to California, Connecticut, Florida, Minnesota, New Jersey, New York, and Vermont, follows many of the concepts included in the "Program Guide" issued by the Public Health Service in 1954. This type of legislation seems to be setting a pattern for other States to follow. Implied in these new programs are more organized efforts by State administration to meet the demands of the public for preventive and corrective services in the mental health field which are equal in quality and scope to general medical services. It recognizes that institutional care of the mentally ill has been designed chiefly for committed patients and does not meet the major needs of early treatment and prevention. The growing emphasis on community services is likely to continue at a rapid pace, greatly increasing the demand for trained personnel, coordination of medical and social services, insurance coverage, and for research on the effectiveness of programs.

State programs were developed by constant teamwork of community, State, and Public Health Service staff, based on the following assumptions:

Poor social adjustment and mental illness is widespread, involving especially children, young adult males, middle-aged females and the aged of both sexes;

Symptom complexes have many causes based on multiple etiological factors, even perhaps in an individual case;
The public is inclined to view mental illness in all ages as a single disease with a "mystical or unnatural" cause. Methods of dealing with the mentally ill are largely responsible for the lack of public understanding;

The public is increasingly concerned with the threat of mental illness, and is extremely interested in prevention. It is interested in utilizing all available knowledge in prevention and treatment programs even though scientific knowledge is limited at present;

There are so many social and economic implications in mental health and illness that the mobilization of family and community resources are essential for an effective mental health program. With more involvement of citizens in educational, preventive, and treatment programs, they would gain a better understanding of the nature of mental illness and of the components of mental health and would be in a better position to support research, training and services.

Current research findings and improved treatment techniques tend to increase rather than decrease the need for more professional staff and organization; and finally,

More effective and complete coverage of preventive, treatment and rehabilitative services would be a tremendous factor in preserving the manpower pool of the nation, in addition to cutting down the morbidity and cost of mental illness.

The increasing interest in healthy psychological development of the child at home and in the school, and his ultimate performance as an adult in a job and as a parent, has made the public acutely aware of the need for corrective services. Besides the general mental health services ordinarily provided, there is increasing demand by organized groups for special services to meet needs for particular areas of distress, i.e., alcoholism, drug addiction, and juvenile delinquency. Maintaining an organization which can integrate staff activity to provide all of these special services and at the same time utilize scarce professional staff most effectively is a challenge to community, State and Federal Governments. There is the danger that States, as well as the Public Health Service, may respond to special areas in mental health programs at the expense of a comprehensive approach, thereby weakening the organizational structure which has been built so patiently in many States during the past ten years. In effect, State leadership responsibility could be scattered again, as it was in 1947.
Another problem is the frequent conflict about who will be responsible for the total mental health program in States. One group demands a Department of Mental Health with Cabinet status, another expects the Health Department to become responsible, and a third group advocates that mental hospitals be given total responsibility. At this time there is insufficient evidence that any one of these ways of organizing State mental health services is the best for all of the States and Territories. Time and experience should help solve the problem and the Public Health Service should advise caution despite the need for stronger and more centralized leadership in some States. In any event, there is little doubt about the need for hospital and community programs to coordinate their efforts in serving people.

The more serious test of whether or not State and community programs will continue to develop in a healthy fashion is still to come. Almost half the States and Territories have considerable dependence on Federal grants for their continued existence. Most of the other States use grants very effectively in testing new methods and evaluating the effectiveness of their programs, which generally would be impossible on State resources. The morale and pace-setting value of grants is extremely important for all States and Territories. With so many pressures for categorical health programs in States, leadership is inclined to stay with those programs that are national in scope.

The shortage of personnel is still serious but not discouraging even though turnover is very great. The Public Health Service regional office staff are more permanent than many of the State program staffs and in many instances they are depended upon to lend continuity to State programs. With State leadership staff struggling to hold on to its gains and to meet the increasing demands of the public for program coverage throughout the State, there is great need for the Public Health Service to continue technical assistance, especially for assessing community needs, introducing new methods, developing new areas of service, and in program evaluation.

If the Public Health Service and the States are to participate effectively in preserving the manpower pool of the nation, so essential to national defense, more suitable and widespread community mental health services, acceptable to the public, must be provided. Practically every professional person in his lifetime will face a serious social or psychiatric problem, either in himself or his family, which will partially or completely incapacitate him in his work for a significant length of time. This time could be shortened if there were convenient and acceptable mental health facilities available which were equal, for example, to the
facilities available for physical disabilities. When physical illness or injury strikes it is usually recognized quickly and facilities acceptable to the family are usually waiting to serve. With mental disorders, it is often the reverse.

The Community Services Branch plans to assist States in holding on to the gains made in community programs by providing mental health consultants in every regional office to give support to State staffs, and assist in getting wider coverage of services to all parts of the State. Specialists in special program areas from within and outside the Public Health Service will be provided to States to help them incorporate the latest practices into their programs. Through technical assistance, conferences will be held with State and community staff for the exchange of knowledge and program development in new areas, especially in the field of alcoholism, drug addiction, school mental health, and aging.

The Public Health Service will cooperate with the State mental health authorities in conducting orientation conferences to acquaint the staff of national, State, and local mental health associations with public mental health programs. These conferences should encourage voluntary and public organizations to work together on common objectives and probably will result also in increased support of official programs by citizen groups.

The staff will work with individuals, groups, organizations, and institutions who are interested in new approaches for prevention, treatment, and rehabilitation of the mentally ill. Besides providing consultation, in some cases, the development of projects will be encouraged. More effort will be given to improving hospital administration and treatment programs. This will be done by providing expert consultants to hospitals, supporting conferences for the exchange of ideas, special studies to improve operating procedures, demonstrations, and small grants to hospital staff members in isolated areas so that they may spend time learning of new procedures in more modern treatment centers.

Demonstrations will be continued in the aftercare of drug addicts, mental health activities in a county school system, and health education in a State mental health department.

Branch staff at the Study Center will continue to study, at close range, one county in Maryland, to keep abreast of community organization and dynamics, and their influence on new mental health services. These studies are important for developing in Branch staff a progressively deeper and sharper understanding of community mental health services, which is so essential for the staff role as consultants to States and local programs.
An effort will be made to assist States in transmitting their training needs to universities. At present, universities tend to emphasize training for clinical services. State and local mental health staffs need training in working with groups and community organizations in the consultation process, training techniques, administration, and research design. Only by communicating their needs to the training institutions can the universities begin to meet the demands of modern mental health programs.

In order to keep abreast of developments in the mental health field and maintain a leadership role, staff will continue to participate in inservice training, in national and regional conferences, and some will have special assignments to States. Staff will also participate in the Public Health Service graduate training program. Next year, Dr. Alan Miller will return from a year's study in England. His special knowledge of the open hospital and how it is integrated in the community will be utilized widely by the Branch. A more complete analysis of State program activities will be made, including scope of program, methods used, effectiveness, cost, legislation, and program activities common to all communities. This information is essential for redefining the role the Public Health Service should play in the expansion of community mental health services throughout the nation. The States have already laid the foundation.

FEDERAL LEGISLATION AND APPROPRIATIONS

No major Federal legislation directly affecting the operations of the Community Services Branch was enacted during the year. The appropriations for grants to States for community mental health services was continued at $4,000,000, as in the previous year, but Guam was added to the States and Territories which share in the grants.

For the first time, appropriations ($2,000,000) were made available for mental health project grants (Title V, Public Law 911) covering the fiscal year ending June 30, 1958.

The total operating budget of the Branch for staff and administration for fiscal year 1958 was $1,116,450, slightly more than a year before.

BRANCH STAFFING

There were 62 professional staff members, plus supporting secretarial staff, employed in the Branch at the
end of 1957. Recruiting additional staff for the Branch was a major, time-consuming activity but was more successful in 1957 than in previous years. Despite the acute shortage of mental health staff, 19 new professional employees were added to the staff. Three professional employees left the staff leaving a net gain of 16 employees. The three staff members who left the Branch were psychiatrists, who are most difficult to recruit.

In central office, a public health physician was employed as a specialist on alcoholism. For part of the year a new psychiatrist worked on industrial mental health before her transfer to a regional office. Also, an administrative assistant was recruited.

The regional offices filled positions for two psychiatrists, two clinical psychologists, two psychiatric social workers and one mental health nurse, helping to complete the mental health teams in the regional offices.

At the Mental Health Study Center, Dr. Alan D. Miller was transferred to England for advanced study and research. Dr. Stanley F. Yolles, formerly the Associate Director is the present Director. In addition, a clinical psychologist was recruited.

The two new demonstrations launched during the year (the New York City Drug Addiction Project and the Volusia County-Florida School Mental Health Project) were able to recruit a full staff complement (six social workers in New York City, a psychologist and nurse in Volusia County). During part of the year, the staff member conducting the demonstration on mental health education in Chic was reassigned to work on the Asian flu program.

As in previous years, the Community Services Branch continued to be responsible for staffing the mental health clinic at the D.C. Juvenile Court on a reimbursable basis. A psychologist was recruited but the position of psychiatrist remains vacant. Plans are being considered for the eventual transfer of responsibility for the clinic to the District of Columbia.

During the year, two psychiatrists on the staff completed training in public health. A staffing innovation in 1957 was the "Career Development" plan. The purpose of this plan is to employ young, promising, fully-trained professional people and provide them with an opportunity to obtain a broader or higher level of experience in order to prepare them to fill the regular positions in the Branch. Under this plan, a social worker was added to the regional office staff and assigned to work as the State-level social work consultant in the Arizona mental health program.

By the end of 1957 there were only ten professional positions vacant and definite prospects or commitments for over half
of the positions. It seems quite likely that in 1958 almost all of the Branch positions will be filled.

In 1958, orientation of new staff will continue to be an important activity. With the completion of the period of rapid growth and expansion, 1958 should see a period of consolidation and, also, the consideration of new ways in which a larger staff can work together effectively.

In the Spring of 1957, most of the central office staff of the Branch moved from the National Institutes of Health grounds in Bethesda to Silver Spring, Maryland. The Hospital Consultation Service of the Branch remained on the Institute reservation. Branch staff recognize the critical space shortage at the National Institutes of Health reservation and also that the physical space available in Silver Spring is superior to the Branch space previously occupied on the reservation. However, the physical separation of the Hospital Consultation staff from the rest of central office staff tends to retard the development of a fully integrated Branch program, despite the strenuous efforts that have been made to maintain lines of communication. Similarly, the staff at Silver Spring have lost many of the benefits of the easily accessible contacts with staff in other parts of the National Institute of Mental Health.

DEVELOPMENTS IN STATE COMMUNITY MENTAL HEALTH PROGRAMS

The major function of the Community Services Branch is to improve, extend, and strengthen State and local community mental health services and mental hospital services. Federal grants to States, mental health project grants, consultation, technical assistance projects, field demonstrations are some of the ways that are used to achieve this objective. A comprehensive program including prevention, clinic and hospital services has been the goal. Of course, progress or lack of progress in individual States and localities result from a complex of factors and forces but the Federal program for mental health services has proved to have significant impact in moving programs ahead.

Plans submitted by States to the Public Health Service show that on the whole, State programs for community mental health services continued to expand in 1957, moving toward meeting the many large areas of unmet needs. Although some States have suffered set-backs, by and large, the coverage and quality of State and local mental health programs are improving. More clinics have been established. Efforts are being made to do more mental health education and to provide consultation to other programs and agencies. In some States, it has been possible to develop and expand a program of training sti-
pends and research. Stronger ties are developing between community and hospital programs. Nationwide, increasing attention is being given to specialized mental health services for particular groups, such as alcoholics, aged, mentally retarded, and patients released from mental hospitals. The regional mental health consultants have had a continuing and important role in working with States on these developments.

Organization

Relatively few changes in organization resulted from State legislation in 1957. West Virginia was the only State that had a major reorganization. The community mental health program was transferred from the Department of Health to the newly created Department of Mental Health which is responsible also for the mental hospitals, the State Training School for the Retarded and the Alcoholism program. Connecticut abolished its Mental Health Council replacing it with a Mental Health Board and gave the Commissioner of Mental Health more authority to direct the program. Idaho changed the size and membership of its Board of Health, and Missouri created a five member State Mental Health Commission responsible for appointing the Director of the Division of Mental Diseases in the Department of Public Health and Welfare.

Divergent organizational changes were made in relation to alcoholism programs. Texas and Utah set up new independent alcoholism agencies. However, two States (California and Indiana) abolished their Alcoholism Commissions and integrated the alcoholism program into the existing public health departments. Illinois created a Division of Alcoholism in its Department of Public Welfare and Washington established an alcoholism program within its State Department of Institutions.

State Grants-in-aid to Localities

Probably the most far-reaching development in 1957 was the legislative action in four States (California, Minnesota, New Jersey, Vermont) which followed the pattern of Connecticut and New York in providing State grants-in-aid to localities for community mental health services.

This type of legislation is highly significant in its impact on the future development of community mental health programs. At the local level, the availability of State matching funds makes it possible for more committees to initiate new programs of community mental health services. Where committees are already completely supporting mental health services, State matching funds release local funds which can be used to expand and improve existing services.

At the State level, the legislation indicates the acceptance by the State of responsibility for helping to finance local mental health services on a continuing basis. State appropriations for community mental health may be expected to increase. An eventual devel-
opment of local services throughout the State is implied. Also State funds act as a binder in bringing closer working relationships of State and local mental health staffs.

The use of Federal grant-in-aid funds is also affected. Part of Federal grants are now being used to initiate mental health clinics in communities. With the availability of State funds for this purpose, Federal funds can be used increasingly for demonstrations of new types of services, pilot projects, training and research.

According to the Minnesota mental health authority, "The recent session of the Legislature enacted the Community Mental Health Act which provides basically for state matching of local funds so that the communities can develop their own local mental health services. Within four years we expect to liquidate the state financed clinics in favor of this community operation. This new program is an example of the use of the demonstration technique. The existing state clinics were established several years ago and their services expanded by the use of Federal funds. They have demonstrated their value and the communities are now willing to share in this cost."

Using a different approach to the development of local community mental health services, three Midwestern States (Iowa, Kansas and South Dakota) authorized their counties to levy taxes or appropriate funds to support local community mental health centers or clinics.

Funds

According to the plans submitted by States to the Public Health Service for the fiscal year ending June 30, 1957, States budgeted $45.4 million of Federal, State, local, and private funds for community mental health services, 76 percent more than a year before. Excluding New York State which accounted for $14.1 million of the total increase of $19.5 million, funds budgeted by the States increased by 28 percent. The largest growth was in mental health clinical services which rose from $18.1 million in 1956 to $37.8 million in 1957.

Of the $45.4 million budgeted in 1957 the large majority (83.3 percent) was for clinical services. Of the remainder, 4.4 percent ($2.0 million) was budgeted for the State mental health program administrative unit, 2.9 percent ($1.3 million) for the control of alcoholism, 2.0 percent ($0.9 million) for training, 1.5 percent ($0.7 million) for research, and the rest for other types of services. Federal funds ($4 million) constituted only 8.6 percent of the total funds budgeted.
State and local community mental health programs have expanded tremendously following the availability of Federal grant-in-aid funds beginning in fiscal year 1948. In 1948, $3 million of Federal funds were available and $2.4 million of State and local funds. In fiscal year 1957, Federal funds had been raised slightly to $4 million but State and local funds had skyrocketed to $41.4 million.

Preliminary tabulations for fiscal year 1958 indicate a continued increase in funds budgeted by State Mental Health Authorities for community mental health services. Available data for 45 States reveal that 34 States have more funds available in 1958 than in 1957 and 11 States have less funds. For the 45 States combined, 20% more funds were budgeted in 1958 than a year before. New York State, which alone spends about half of the total funds budgeted in the nation, reported a tremendous increase of $6.4 million between 1957 and 1958. Other States reporting large increases included Alabama (74%), Delaware (53%), Louisiana (30%), Ohio (40%), Oregon (83%), West Virginia (121%), and Wyoming (84%). States reporting decreases included Kentucky (10%), New Mexico (18%), Washington (15%), and Puerto Rico (42%).

Three States (Colorado, Washington, Wyoming) for the first time in 1957 voted specific State appropriations for community mental health services, thus joining the large majority of States which already have identified mental health appropriations. Such action by a State legislature is concrete recognition of the State's responsibility for community mental health services, and usually sets a precedent for additional and more adequate appropriations in future years.

Staffing

The development of strong State-level mental health teams to provide leadership in the States has been a long-time objective of the Branch. The Branch has especially encouraged a basic State level team which includes representatives from the four mental health disciplines of psychiatry, clinical psychology, psychiatric social work and mental health nursing. During 1957, States slowly expanded their State-level mental health staff. At the end of the year, 12 States and Territories had State-level teams representing the four disciplines, 18 States had teams representing three disciplines, and 24 States had representatives of only one or two disciplines. In some States, only part-time services of staff were available.

As of December 1, 1957, there were State level psychologists carrying administrative or consultative responsibilities in community mental health programs in 29 States, psychiatric social workers in 40 States and mental health nurses in 27 States. Three States (California, Maryland, New Hampshire) passed laws on certification of psychologists. Several States (California, Georgia,
Pennsylvania, Texas) are developing regional staffs of psychiatric social worker consultants who serve several counties within a State. Several States have increased State-level nursing positions (e.g., Florida, Kentucky, Massachusetts, New York, North Carolina). Vacancies for personnel in State and local positions continue to increase faster than such personnel are being trained.

Heavy turnover in the top-level State staff continued to plague mental health programs. Almost one-third of the States and Territories had changes during 1957 in the directors or commissioners of community mental health programs (Colorado, Connecticut, District of Columbia, Georgia, Idaho, Indiana, Kentucky, Missouri, North Dakota, New York, Ohio, Pennsylvania, Puerto Rico, Utah, Virginia, Virgin Islands, West Virginia). Without attempting to evaluate whether the staff changes strengthened or weakened State leadership, the fact of change alone interrupts the continuity of program. Also the high "mortality rate" in these top jobs tends to deter many high caliber, career-minded people from seeking positions in State service.

Mental Health Education and Consultation

All States have programs of mental health education and consultation for lay and professional groups and agencies. To brief general practitioners in the diagnosis and treatment of mental disorders as well as in referral processes, Nebraska is using Federal funds to develop a special film for this purpose. Federal funds are also being used in a Bridgeport, Connecticut mental health clinic to experiment with the employment of a psychiatric social worker in a position called "Educational Director."

Local Services

New local mental health centers or clinics continue to be organized (e.g., Alabama, Illinois, Massachusetts, New Hampshire, New York, Ohio, Tennessee) but sparsely settled areas have great difficulty in recruiting staff. Clinic services are especially scanty in large areas in the South, Southwestern, and Mountain regions of the country. According to the Oregon Public Health Service plan, "The most vociferous demands in the field of mental health are for increased mental health clinical services for both adults and children." Some States are using traveling clinics, some are trying to organize multi-county clinics, and others are trying to provide mental health consultation services where no direct treatment facilities are available.

To meet the need in rural areas, Florida has evolved a new kind of mental health staff person called a "mental health worker." These "mental health workers" (whose background may
have been in nursing, teaching or social work) are stationed in the rural counties. They refer people to the clinics in the urban counties and try to carry out the recommendations made by the clinics in conjunction with community agencies. They also conduct a program of mental health education and community organization. The program of the "mental health worker" has received strong legislative support in Florida, and the idea may spread to other States even though the effectiveness of the plan has not been established. Alabama, for example, has indicated that it is seriously considering initiating such a program in 1958.

**Mental Retardation**

State legislatures showed high interest in mental retardation. Idaho and Minnesota made it mandatory for local school districts to provide instruction for handicapped children. State funds were appropriated for the establishment of a diagnostic and training center for the mentally retarded at the University of Washington. The Delaware legislature authorized the establishment of day centers for children with an I.Q. of less than 35, who are living with their families. New York is making a State-wide census of mentally retarded children and will be developing plans for a State research institution on mental retardation. Massachusetts received a new appropriation of $150,000 for community nurseries for retarded children.

Examples of mental retardation projects, which are supported by Federal grant-in-aid funds, include the multidisciplinary training program of the New York Medical College at the clinic for the mentally retarded of the Flower-Fifth Avenue (New York City) Hospital, and the day care program for young mentally retarded adults of the Retarded Children's Aid Agency of Chicago. In many States (e.g., Arizona, Nevada, Oklahoma, Rhode Island) State mental health staff have been actively involved in the establishment and development of new clinics for the mentally retarded which are supported through Children's Bureau grants.

**State and Local Surveys**

Surveys of State or local mental health needs and resources are another indication of the stir and ferment on mental health. The American Psychiatric Association completed surveys of Iowa and Ohio. State-wide surveys are planned or underway in Michigan, New Hampshire and Nevada. Los Angeles, California, and Montgomery County, Maryland, are examples of the more numerous local communities in the midst of a survey.

**Training and Research**

Training and research were being stepped up through the action of State legislatures. The Iowa legislature set up a new
fund for training and research at the Psychopathic Hospital. The appropriation for Florida's Council on Mental Health Training and Research was raised to $363,000 for the current biennium as compared with $250,000 in the previous period. Texas will be organizing a new community hospital for training and research in mental illness, to be located near the Texas Medical Center in Houston. In 1958, Illinois will be opening its new training and research center, the Illinois Psychiatric Institute in Chicago. Louisiana appointed a new Director of Training and Research and got its new training program in operation, after making agreements for the training of mental health personnel with Louisiana State University, Tulane University and two State hospitals. The Medical Center at the University of North Dakota was directed by the State legislature to encourage the training of psychiatric personnel for staffing the mental health agencies of the State and training stipends were provided.

Alabama made its first effort to attract mental health trainees to the State when it set up a training unit in Birmingham. Massachusetts has set up a project for training community mental health staff. A curriculum is planned for public health nurses, school psychologists and school social workers. Also, by offering second-year fellows in child psychiatry, part-time experience in the mental health center program, the Massachusetts Department of Mental Health hopes to interest more of them in the community mental health field. Under the Division of Community Mental Health Services in New York, about 50 stipends are being awarded to mental health trainees; about 45 stipends to employees of the mental hospital program. Indiana will be using about $50,000 of its Federal grant-in-aid for training stipends.

Sparked by a consultation request from a State, a staff member of Region II, with the cooperation of staff in other regions, conducted an informal survey of the educational leave policies for psychiatric nurses in State mental health programs in June, 1957. The survey revealed a paucity of State financial support for the professional training of psychiatric nurses. Of the 44 States reviewed, only 12 had State funds available for training stipends. These 12 States were: California, Florida, Illinois, Kentucky, Louisiana, Michigan, Minnesota, New York, Ohio, Pennsylvania, South Carolina, and Virginia. The level of training supported by the States varied and ranged from single courses to training for the Master's degree. Without exception, everyone of the 12 States expected the trainee to accept State employment for a specified period in return for the financial aid provided during training.

A second staff member in central office supplemented this survey with a narrative report which included a discussion of the problems resulting from the frequently inadequate
amount of the stipend and from the requirement for obligated State employment in return for the training stipend.

In the area of research a program of research in alcoholism was established at the College of Medicine of Ohio State University. The California Department issued its first research report on a study which found that there are few patients arriving at the State mental hospitals who could be cared for better in an outpatient clinic. The General Bacon Health Center in Delaware is working on a study of the relationship between behavioral adjustment and the emotional arousal pattern in children. The Michigan Department is conducting an analysis of the characteristics of audiences participating in mental health education programs. Minnesota is supporting a study of the reasons for the breakdown of recovered or partially recovered mental patients. New York is studying schizophrenic children in outpatient settings.

In its official plan submitted to the Public Health Service, Connecticut reported that, "A grant of Federal funds was made in 1956-57 to a psychiatric clinic for children in Bridgeport to enable its staff to do a preliminary survey and evaluation of some of the work done in that clinic over a five-year period. As a result of this preliminary survey, the clinic expects to undertake some more intensive research activities in the coming year supported by funds from other sources."

During the year a member of the Region V staff issued a compilation of mental health research conducted or supported by State mental health agencies in that region during 1956-1957. Of the 122 research projects reported, 46% were biological, 33% clinical, and 21% were psycho-social. Fourteen of the projects were in mental retardation and five were on aging.

Needs

Although progress is being made on many fronts, the States report many gaps and inadequacies in over-all community mental health services. In the plans submitted to the National Institute of Mental Health, State after State indicates the need to set up more mental health services for people living in geographical areas now without services. States are seriously concerned with the need for more treatment and rehabilitation services, mental health education, consultation to community agencies, training opportunities for mental health staff, and research and evaluation. Over and over again States report that the bottlenecks are inadequate funds for community mental health services, shortages of professional mental health personnel, and low salaries.
MENTAL HOSPITALS

Mental Health Project Grants

A major effort of the Hospital Consultation Service of the Branch has been in providing staff services to the new Mental Health Project Grants program. Legislation establishing this program was passed by Congress (Public Law 911) in 1956. This legislation was based upon the recognized need for encouraging effective ways to improve programs for the care of the mentally ill, for experimenting with new methods of care, and for helping isolated hospitals to demonstrate the feasibility of methods already successfully in use elsewhere. It was believed that, in many instances, the secondary gains to the institution because of the stimulation of working on a project would in itself improve the quality of care in that institution. When Public Law 911 was passed, no appropriation was made. However, steps were taken to establish the groundwork for the grants program. A Review Committee was established with a membership of thirteen outstanding professional persons from the field of psychiatry, clinical psychology, psychiatric nursing, psychiatric social work, sociology and hospital administration. Applications were received beginning in January 1957 in anticipation of the availability of funds. The response to the announcement of the grants program was enthusiastic and immediate. Two million dollars were made available for grants during fiscal year ending June 30, 1958.

The Review Committee has met three times during 1957 and has considered 137 applications. Applications have been received from 34 States and three Territories, including States in every region of the country. Organizations submitting applications have included State departments of mental health, State hospitals, State institutions for the mentally retarded, private hospitals, clinics, universities, residential treatment centers for children, rehabilitation centers, and professional organizations.

To date 44 projects totalling $1,385,306 have been approved by the National Advisory Mental Health Council. Examples of the initial projects which are just now getting underway are:

1. Demonstration of a day hospital service in a child guidance center setting.

2. Demonstration of a special group program for acting-out children in a residential treatment home for children.
3. Demonstration of a day hospital program for psychotic children, as part of the state hospital unit for psychotic children.

4. Utilization of a public health nursing service in the supervision of convalescent psychiatric patients.

5. Coordination of community services to facilitate the hospitalization of patients.

6. A study of preadmission services and alternatives to hospitalization.

7. Establishment of aftercare services and the coordination of community services in a rural area.

8. A study of the various techniques for the care and treatment of chronic psychotic patients.

9. The improvement of medical records in a large state hospital.

10. The provision of comprehensive psychiatric services in a geographically isolated area with maximum utilization of local facilities.

11. A project to develop ways and means to sustaining the geriatric patient extramurally and cut down, if possible, the admission of the nonpsychotic geriatric patients to the public mental hospital.


13. Demonstration of a psychiatric rehabilitative service for young inmates of a county jail.


15. A demonstration project which would set up a suicidal referral service in a large urban area.

16. A study of the role of practical nurses as a possible solution to the problem of the shortage of nurses in state hospitals.

It can be seen that the approved projects cover a wide range of problems in intramural and extramural care.

In the course of the review and approval of the projects, the Review Committee has been working on guide lines for the program. Early in 1958 the Committee plans to review the progress
of the program and to see if there are uncovered areas which are in need of further stimulation and development.

As in many new programs, the working out of relationships has been an important factor in the initiation of this program. This had included the clarification of the responsibilities between headquarters and regional office staff. Some questions have come up concerning the confidentiality of grant applications and the role of the State mental health authority in relation to applications from voluntary agencies. Efforts have been made to interpret the basic features of the Mental Health Project Grants program.

Headquarters and regional office staff have received numerous requests for consultation concerning the program. The staff members and members of the Review Committee have made site visits and have given consultation. Applicants have indicated that these consultations have been most helpful in clarifying the potentialities of their own program as well as stimulating the development of better patient services.

Currently approved projects will require over $1,200,000 of grants in order to continue in fiscal year 1959. Unless additional funds are available, very few new projects can be added during fiscal year 1959. The staff will make visits to the approved projects and will be available to help project directors in their recruitment of personnel and in their working out of the projects.

Hospital Consultation

The year 1957 has seen an acceleration in the amount of consultation given to State hospital programs. The regional office consultants as well as the staff of the Hospital Consultation Service have been active in this area. The Hospital Consultation staff have visited 36 states to meet with hospital and other mental health personnel and to visit mental health facilities. Through these visits new program ideas are being communicated widely. The content of these consultation visits covered a wide variety of subjects and some new patterns in the care of mental patients seem to be spreading rapidly.

Several States attempted to modernize their laws in regard to the commitment, detention and care and treatment of the mentally ill (e.g., California, Colorado, Kansas, Minnesota, Montana, North Dakota, Texas). Alaska enacted a comprehensive mental health act following the framework of the Alaska Mental Health Enabling Act passed by the Congress.

Of special interest was the 1957 legislative action in seven States (Connecticut, Maine, Minnesota, New Hampshire, Oregon, Rhode Island, West Virginia) which ratified the Interstate Compact on Mental Health. Together with Massachusetts, New Jersey, and New York which ratified the Compact in 1956,
ten States are now participating in the inter-State agreement which was first issued in 1955. The Compact makes the patient's welfare the cardinal consideration in deciding whether he shall be kept in one State or sent to another. The prompt action of the ten States suggests that the Compact meets a long recognized need and also that inter-State agreements may be a useful administrative device for helping to solve other problems of providing mental health services.

The establishment of psychiatric facilities in general hospitals seems to be a definite trend. For example, Georgia asked for help in developing its program for establishing such units and using them as screening centers for patients prior to admission to the state hospital. The State plans to reimburse the local hospitals for the care of the patients.

The philosophy of the "open hospital" is receiving widespread attention. This philosophy implies the creation of a therapeutic milieu, greater patient freedom, a different conceptualization of the status of the patient with, in turn, differences in the staff-patient relationships, a fuller integration of the hospital into the community, and a broader use of community resources. Most hospitals are trying to achieve this goal one step at a time. Mental Health Project Grants are being used by a few hospitals for this purpose.

Many hospitals are asking for help on how to achieve improvements in patient care with "what they have at hand now" and without either extensive building programs or recruitment of hard-to-get professional personnel.

Several States are taking action to provide special care and treatment for emotionally disturbed or psychotic children. The Minnesota and Virginia legislatures authorized the establishment of resident treatment centers for emotionally disturbed children while Nevada and Washington will be establishing special treatment facilities for children as part of the State hospital program.

Interest and activity in mental retardation continued at a high level. Arkansas, Nebraska, Texas, and Wisconsin authorized the construction of new institutions for care and treatment of the mentally retarded.

Aftercare facilities and programs are becoming increasingly important. These are being developed as a part of hospital programs and as a part of community programs administered by voluntary or public agencies. Two conferences on aftercare were held as Technical Assistance Projects and involved participation of regional and headquarters staff. Three regional conferences were held with the Office of Vocational Rehabilitation and mental hospital personnel on the rehabilitation of the mental patient. These were held in Regions IV, V and VI. Another conference in California enabled the
hospital and aftercare staff to meet together. All of these conferences have contributed to the better understanding between the intramural and extramural programs and better communications in the interests of patients.

The half-way house as a method of care is receiving widespread attention and interest. As in any new development, there is much experimentation and considerable variation in the various programs. Some see the half-way house as meeting a need for an interim facility which avoids the dependent security of a hospital ward and yet offers an individualized as well as a group program. It is possible that in some communities the already established facilities, such as the YWCA and the YMCA, may provide this kind of opportunity for the discharged patient. Some hospitals are setting up rehabilitation wards that provide interim care to the patient and assist him in his integration back into the community. Patient clubs or social therapeutic clubs are becoming more widespread and are another assist to the patient in his resocialization.

The interest in the development of half-way houses and patient clubs is very closely related to the growth in scope and importance of the volunteer movement. Volunteers are an important factor in the closer working together of hospitals and communities. Volunteers are being used in many roles in working with the institutionalized patients and are sponsoring some community efforts such as ex-patient clubs and half-way houses. A conference on the work of volunteers with mentally ill patients is to be held in June 1958 under the sponsorship of the American Psychiatric Association and four other national organizations. This conference is being supported by a grant from the National Institute of Mental Health. Four preparatory commissions are gathering material to be used as the basis of the conference. This conference will consider the present status and purposes of volunteer programs for the treatment, care, and rehabilitation of the mentally ill; the delineation of the functions of volunteers; the unique programs in the field of community rehabilitation services; and the existing administrative patterns and personnel policies governing the operation of volunteer programs. Problems of recruitment and training of volunteers will also be considered.

The care of the aged in nursing homes and in mental hospitals is getting increased attention nationwide. Crowding in other community facilities often makes the State hospital the only place for the disabled old person. In some States, county homes are used for this purpose. Visits have been made by staff to the county homes in two Mid-Western states and a workshop is to be held in December 1957, with nursing home operators in another State. Branch staff are participating in the planning of a national conference of nursing home
operators in February 1958, which is being sponsored by the Bureau of State Services, Public Health Service.

The community care of the mentally ill and the early discharge of patients from State hospitals together with treatment in the community in lieu of hospitalization have many implications for other community health and welfare programs. Consultation has been provided to national and State agencies on ways of coordinating services of hospitals, public health and welfare agencies. Community workers such as public health nurses and welfare workers are key figures in providing care for the patient and his family. Many efforts are being made to familiarize these workers with the problems of the mentally ill, and to interest them in expanding their services to this group. There are also indications of the need for change in agency policies which may exclude a person from service by reason of his mental illness. Conferences have been held with personnel in the Bureau of Public Assistance and Old Age and Survivor's Insurance to point up some of these questions. The fact that the American Public Welfare Association devoted part of its "Round Table" to a consideration of the problems of mental health and mental illness, is a very encouraging indication of the interest of welfare administrators in this area.

The upgrading of the existing staff through staff development activities and the use of the psychiatric hospital as a training resource have important implications for improvement of patient care. The Hospital Consultation Service staff have contributed to a number of different kinds of staff development efforts, including regional meetings, summer institutes, hospital staff seminars and staff consultations. Special consultation was given to one State concerning the development of its hospitals as training centers.

It has not yet been possible to work out adequate information collection procedures in order to answer the requests for information on such subjects as State commitment laws, State licensing laws for private mental hospitals, architectural plans, trends in aftercare programs and personnel standards. It is hoped that during the coming year further progress can be made in the collection and analysis of such data.

One of the needs voiced by many States is for small amounts of money with which they could initiate a variety of developmental projects. Such money could be used for consultation, for staff development, for sending staff teams to visit other hospitals, or for experimental purposes. It may be that this need can be met through the Mental Health Project Grants Program; if not, ways need to be found to assist States in this kind of effort.

SPECIAL AREAS OF MENTAL HEALTH

Alcoholism

Branch activities relating to alcoholism during the past
year have expanded in two important respects. The first is the increased amount of service given by the regional mental health staffs to program developments relating to alcoholism. The rising number of requests for such services reflects a growing awareness of the relatedness of alcoholism to the broad field of mental health problems. Regional staff were being asked to meet the following kinds of requests: planning for and participating in State or regional institutes on alcoholism; development of more effective treatment and rehabilitative measures in State mental hospitals and mental health clinics; consideration of alcoholism in relation to tuberculosis, diabetes and other chronic diseases; problems of alcoholism in industry; consideration of excessive drinking among Indians. Regional mental health staff also consulted with other regional staff of the Public Health Service and of the Department (such as the Office of Vocational Rehabilitation) on problems of alcoholism.

There are currently 37 official State alcoholism programs in operation, with others in various stages of organization. A commonly cited factor relating to these programs is that they have relied entirely on State initiative rather than on Federal support. The desirability of effecting more formal working relations between these presently independent programs on alcoholism and the Federal-State operations pertaining to other public health activities, is a matter now receiving attention on both State and Federal levels. Regardless of the nature of such a relationship, it is practically inevitable that the participation of the regional mental health staffs will continue to grow in significance.

The return of Dr. Paul H. Stevenson to active duty as Consultant on Alcoholism marks the second advance during the year in the Branch's activities relating to alcoholism. This event provides for more effective consultation services to and through the regional office staffs and also for the reactivation of certain headquarters activities. Most important will be the renewal of active liaison relations with the major organizations operating on the national scene in the field of alcoholism, and the maintenance of rosters and current summaries of State and local programs and facilities, thus serving again as a clearing house for information. In addition, through the procurement of the recent annual issues of the Classified Abstract Archive of the Alcohol Literature, the Institute is now one of the limited number of depositories of this service in the country. This archive will be kept current, and arrangements made to make it available to a wide circle of research workers and program staff working in the field.

In March 1958, the National Institute of Mental Health and the Bureau of State Services, Public Health Service, will jointly sponsor an ad hoc conference of about 25 national ex-
erts in the field of alcoholism. They will be asked for their suggestions on the future role and program of the Public Health Service in regard to alcoholism.

**Industrial Mental Health**

At the 1956 Conference of the State and Territorial Mental Health Authorities with the Surgeon General, the mental health authorities requested that the National Institute of Mental Health make available information dealing with mental health in industry. For several months in 1957, a Branch psychiatrist was assigned to work in central office on mental health in industry. This staff member prepared the publication, "A Review of Mental Health in Industry" which contained a review of the literature, a bibliography of some 150 titles, a description of several programs in large companies, and a list of films on human relations in industry. The review of the literature covered recent history, functions of the psychologist and psychiatrist, relationships of mental health programs to general industrial health programs, attitudes of management and labor, and training and research. The special problems presented to industry by absenteeism, accidents, alcoholism, and the elderly worker were also considered. The review found that the participation of public health agencies in the industrial mental health field has been limited and fragmentary and suggested the need for development and expansion of the total field of mental health in industry.

**Mental Retardation**

A member of the central office staff was the joint author with Dr. Seymour B. Sarason of a major report (in press) on mental retardation. The report entitled, "Psychological and Cultural Problems in Mental Subnormality, A Review of Research," was sponsored by the National Association for Retarded Children under a National Institutes of Health grant.

The report points out that the bulk of cases of intellectual deficit are identified and become problems during the span of years children normally attend school. Therefore, reported prevalence of retardation in the population reaches its highest point at age 14-16. These children and adolescents who have been labelled retarded leave the school system and merge successfully into the adult population because their post-school life places different kinds of intellectual demands upon them. There is no present reason to assume either organic or hereditary etiology in most of these individuals; rather, they suffer from learning deficits often introduced by the subcultural patterns of living and child rearing characteristic of the groups into which they were born. The report urgently recommends research on the nature of the intellectual processes learned in the various sectors of our population, on better means of identifying learning deficits at
the preschool level so that corrective action may be taken before it is too late, and on the intellectual requirements of social living outside of the school situation.

Narcotic Addiction Demonstration

A Demonstration Center to work with drug-addicted patients discharged from the Lexington Hospital was launched by the Community Services Branch during the year. The Center was set up in New York City in an attempt to prevent relapse among discharged drug addicts by helping them utilize the facilities of community health and welfare agencies and by providing consultation to the agencies so that they will better be able to meet the needs of former addicts. The program of the Center is based on the general premise that an increased use of community resources will help to rehabilitate narcotic addicts. Experience has shown that there are obstacles both in the patient and in the community that interfere with the full use of community services for this group.

A staff of six psychiatric social workers has been employed and arrangements have been made for part-time psychiatric consultation. The Center staff have been contacting community agencies and, somewhat surprisingly, have found that agencies are willing to cooperate with the Center and to provide service to selected addicts. In many instances, this has involved a reversal of previous agency practice.

The Center will also be continuing a previous project of the Bureau of Medical Services, Public Health Service, to maintain contact with a sample of drug addicts, without attempting treatment intervention, in order to find out about re-addiction rates after discharge. In addition, a study is being planned of the social and psychological factors that distinguish those who successfully discontinue taking drugs from those who become re-addicted.

School Mental Health

The number of school mental health activities of the Community Services Branch increased in 1957 in response to greater interest in this area by the States and the greater emphasis given these programs by our staff. The year 1957 is the first time the Branch has had a full-time consultant working in this special area. The provision of a full-time consultant in this field enabled the Branch to work more closely with other Branches of the Institute also involved in mental health in education activities and to provide increased consultation to national organizations, States, and teacher-training colleges.

Colorado, Mississippi, Idaho, Missouri, and South Dakota, were among the States which utilized Branch staff
to develop joint conferences of State mental health and education personnel on school mental health program development. Region III reviewed the school mental health activities of its States as a part of a regional study of school health programs. Seventeen Southern States under the Southern Regional Education Board initiated a project to increase the utilization and training of school psychologists. Considerable effort was expended on establishing closer liaison with the Office of Education, Department of Health, Education, and Welfare, and the National Education Association.

During 1957, the Branch, in cooperation with the Florida State Department of Health and Education initiated a school mental health demonstration in Volusia County, Daytona Beach, Florida. Two members of Branch staff, a clinical psychologist and mental health nurse, were assigned to this county to study the present and potential local health department's school system teamwork on the screening and local management of minor emotional problems in school children. It is anticipated this study will help to formulate the elements of a basic school mental health program that can be adapted and field tested for use in other rural counties.

**TECHNICAL ASSISTANCE PROJECTS**

Technical assistance projects were initiated in 1955. These projects are special conferences focused on a particular mental health problem of a State. They are designed to assist the States in building their mental health programs and are seen as an extension of the consultation and technical assistance now provided to the States through the professional staff of the Community Services Branch. They have been particularly valuable in helping States explore and develop new mental health program areas.

In 1957 there were 12 technical assistance projects carried out as a joint endeavor by the States, Regional Offices, and the Branch, at a total cost of approximately $45,000. This represents an average cost per project of approximately $3,700. Generally, at least one outstanding national consultant is employed to participate in the project. The following is a listing by title of the projects carried out this year:

- **California** - "Coordinating Treatment Services for Mental Patients in California"
- **Colorado** - "Development of Better Social Services--Family, Patient, Hospital, Community"
- **Colorado** - "Mental Health Through Coordinated Efforts of Education, Mental Health and Public Health Personnel"
Connecticut - "Applications of Management Theory to Administrative Psychiatry"

Iowa - "Rehabilitation and Post-Hospital Care for the Mentally Ill"

Mississippi - "The School, the Child, and Mental Health"

Missouri - "Leadership Training for Community Mental Health Promotion"

New York - "In-Patient Psychiatric Units for Children - A Program Designed to Prepare the Child for Return to the Community"

Pennsylvania - "Conference of Community Mental Health Clinics"

South Dakota - "Leadership Training for Mental Health"

Texas - "Maximum Utilization of Community Agencies in Treating Emotionally Disturbed Children"

Utah - "Development of Collaboration between State Agencies to Promote Better Mental Health Programs"

CONFERENCES OF CHIEF STATE PSYCHOLOGISTS, SOCIAL WORKERS, AND NURSES

As in previous years, Branch staff helped to sponsor and plan conferences for top State-level community mental health staff in each of three disciplines: psychology, social work, and nursing. These conferences provide an opportunity for the State staff in one discipline to exchange ideas and information on program developments in the various States. The meetings of the chief State psychologists focused on the need for psychologists to have training in consultation and administration. The social workers' meetings discussed the philosophy, methods, and techniques of mental health consultation. At the nurses meeting, resource books, containing mental health materials and publications of special interest to State-level nursing consultants, were distributed. Several members of university nursing faculty, who were present at the meeting, requested copies for their use in teaching. The shortage of mental health nurses was a major subject of discussion.
ORIENTATION COURSES FOR COMMUNITY MENTAL HEALTH

In accordance with recommendations made by the 1956 Conference of State and Territorial Mental Health Authorities, the Community Services Branch has assigned two staff members to be responsible for developing a course of instruction and orientation on community mental health programs for State-level mental health staff. Following completion of a preliminary plan for such a course, an advisory committee will be established, including representation from the Community Services Advisory Committee, members of the National Institute of Mental Health staff at headquarters and regional offices, and consultants outside of the Public Health Service.

It is anticipated that an initial pilot course will be given for the States in three regions where the problems are fairly similar. Emphasis in the course will be placed on program planning, coordination of community agency activities, and administration. Experienced people from State mental health program staffs, as well as others, will be drafted as faculty members to discuss and present aspects of these problems.

It is planned to have this first course early in 1958; a second course in another area of the country is planned for the Spring of 1958. Later courses may provide more intensive training in special areas, such as administration. Where possible, such subsequent units will probably be arranged through contracts with appropriate university graduate departments, schools of public health, graduate schools of social work, etc.

REPORT ON FEDERAL MENTAL HEALTH ACTIVITIES FOR CHILDREN

At the request of the Joint Commission on Mental Illness and Health, a statement was prepared on the impact of Federal mental health activities on services for children. Although the statement focussed primarily on activities of the National Institute of Mental Health, the review revealed the tremendous range of activities and the substantial investment of the Federal government in the mental health of children. A surprising number of Federal agencies are active in this field, including the Cooperative Extension Service of the Department of Agriculture, Department of Defense, Bureau of Public Assistance, Office of Education, Children's Bureau, Department of Justice, and many programs of the Public Health Service.

Within the Community Services Branch, activities directly related to children included the following: (a) About 10% of the time of regional consultants was devoted to school mental health, (b) a psychiatrist is assigned full-time to work on school mental health, (c) a school mental health demonstration has been launched in Volusia County, Florida, (d) four of the twelve technical assistance projects conducted in 1957
were directly concerned with children, (e) Federal grants-in-aid for community mental health services have helped State programs grow from $2.4 million of State and local funds budgeted in fiscal year 1948 to $41 million in 1957. Federal grants have been an important factor in the tremendous spurt in the number of outpatient psychiatric clinics established since 1946. Preliminary tabulations reveal that 72% of the persons served in outpatient psychiatric clinics were under 18 years of age. Federal funds have been used in many States for "growing edge" activities for pilot projects, experimental services, demonstrations, and research. A frequent pattern is the use of Federal funds to demonstrate a new mental health service which, after the success of the demonstration, is taken over and supported by State and local funds, (f) under the National Health Project Grants program (Title V), eight projects totalling $278,000 (October, 1957) were approved which were concerned with children.

CONSULTATION ON RESEARCH AND EVALUATION

Increasingly, as programs in State mental health agencies expand and develop, requests are made for consultation services relating to program research and evaluation. With the pioneering stage passed, interest has turned to justification of existing programs and increased evidence that services are actually accomplishing the results for which they are intended.

To supplement resources in the regional offices, during the past year a Section on Program Research and Evaluation within the Community Services Branch was established in central office. Two staff members are presently serving in that capacity. Regional consultants can request assistance from this Section as occasions and problems warrant. Also through this Section, the various technical research resources in the many laboratories and branches at the National Institute of Mental Health may be made available to the regional offices and State mental health programs.

As an illustration of the activities of this Section, at the request of the mental health consultants in Region VIII, the two staff members of the Section participated in a meeting held in Utah to consider possible research studies relating to the establishment of new communities. This meeting was sponsored by the Bureau of Mental Health of the Utah Department of Public Health and included representatives from the Departments of Psychology, Sociology, and Anthropology in the three State universities -- namely, the University of Utah, Brigham Young University, and Utah State University. This planning group is interested in a large-scale, long-term study of three new towns being built near the Utah-Arizona border in connection with the construction and use of the Grand Canyon Dam. Also,
a fourth town similarly related to the Flaming Gorge Dam on the Utah-Wyoming border may be included. Any such studies would be multi-disciplinary and would involve all three universities.

Questions were raised and discussed with reference to Public Health Service research grants, administrative problems within the university, collaboration, research design and grant procedures.

THE MENTAL HEALTH STUDY CENTER

The Mental Health Study Center, a field station of the Community Services Branch in Prince Georges County, is a clinical unit whose general function and purpose is to provide a setting in which studies can be conducted on various aspects of community mental health. It functions in four major areas, operation: (1) a research program ranging from studies on the structure, function, and operation of mental health units to epidemiological studies of problems in community mental health; (2) a mental health consultation service for Prince Georges County service agencies concerning family problems and community mental health activities; (3) a limited all-purpose psychiatric outpatient service restricted to residents of Prince Georges County; and (4) in addition, the Center engages in training activities for various professional personnel. The staff of the Center are also called upon from time to time to act as consultants outside of the County.

Epidemiological Study of Reading Disability

This project is now in its fourth year. It is a product of the basic interest in the problem of locating emotionally disturbed and maladjusted individuals in the community and in identifying some of the psychological and sociological factors associated with such maladjustment. As a resident mental health research team that also offers service in the county, the staff became aware that one major concern, in the schools, in the homes, and in the courts, was the apparent high frequency and ubiquity of serious reading problems among children. The staff recognized that this community problem was remarkably suitable for epidemiologic inquiry. Reading disability is a definable phenomena. Accurate and complete case finding, one of the more difficult problems in epidemiologic studies of mental disorders, is an approachable goal. It is possible to know with reasonable accuracy how many children have serious disabilities, to know where these children live, and if only crudely at first, who they are and how they live. It is also possible to know these things about average readers and good readers.

In spite of the fact that this phenomena is defined in educational terms, it is almost certainly of great mental health relevance. The syndrome of reading disability is clearly a
final common pathway which may have many origins. Reading is a basic and highly valued communication skill and a dis-
ability in this area, whatever its origins, limits the in-
dividual's capacity in many areas. As with so many chronic
disorders, the consequences reduce the probability of its
correction and may, in fact, lead to its entrenchment and
even enhancement. The staff are interested in exploring
and documenting this apparent destructive potential. It is
the impression of the staff that such a disorder, together
with its sources, constitutes an important reservoir of
psychopathology from which a variety of disorders may e-
merge. Should this be demonstrated, the presence of read-
ing disability in an individual or an unexpectedly high in-
cidence of reading disability in a family or neighborhood
or community could serve as a flag calling attention to the
need for more intensive examination. This may be, in short,
something like a "coliform count" for a public health
screening device for mental health problems. The staff ap-
proach to the problem is a multi-dimensional one; some of
the areas of interest are described below:

a. A profile of reading performance by school dis-
trict will be completed during the first half of 1958 based
on data collected over the past three years. Earlier inter-
im studies have demonstrated the reliable performance of
most school districts as well as increasingly reliable differ-
ences between discreet geographical and sociological units
in the county. The profile will provide a basis for the
study of the meaning and significance of these differences
as well as offer some clues to the nature and direction of
performance changes in specific localities and in the county
as a whole.

b. A series of longitudinal studies based on three
years of data from 1954 to 1957 will be completed during the
winter of 1957-58. These studies provide a crude sampling
of children along a broad spectrum of reading achievement
and covering grades one through nine. They describe, with-
in sampling limits, a picture of the range and variability
of reading achievement over these grades. The three stud-
ies have provided a good estimate of the reliability of the
data-collecting instruments including the "reading quotient,"
a statistic that permits comparison of reading achievement of
children at different age levels. They will also permit the
evaluation of impact of age, sex, and certain psychological
and socio-cultural forces on achievement.

These longitudinal studies will also serve as pilot
projects for a Cohort Study of the entire sixth grade school
population of 1954-55 (approximately 5,000 children), to be
started during 1958. This study is planned first as a test
of the hypothesis that reading disability identified early can act as an indicator of psychopathology. In addition to collecting data on the total school careers of this group, information will be gathered from the Health Department, the Courts, Welfare Department, and other community sources. Second, and perhaps more importantly, the study will allow the development of methods for the effective and meaningful handling of large amounts of individual mental health data.

c. The clinical study of the first group of boys with reading disability and of their parents was completed during 1957 and a second group has been in treatment for eight months. These intensive studies of families seen in collaborative group therapy have contributed heavily to staff understanding of the intra-personal, familial, and cultural dynamics that appear to be so significant in this syndrome. One of the methods of dealing with the problem may be collaborative group therapy, a by-product of the research operation.

d. Current plans, in addition to the Cohort Study, call for the completion of the survey of individual and family life, originally planned for 1957 and postponed. This survey will seek to examine the social matrix in which the syndrome appears through surveys of individual and family life in several of the communities pinpointed as high and low incidence areas by the demographic study.

Post-Hospital Project

This project, begun in 1955, is a survey of a group of mental hospital patients returning to their homes in Prince Georges County. It was felt that people who had experienced hospitalization could contribute to the understanding of adjustments during the post-hospital period. This information could be useful in planning for service programs for the post-hospital patient.

During the twelve-month period of August 1955 through July 1956, 77 patients returned to the county. Forty-six of the 77 were interviewed; 24 had moved, 4 were not available for interview and 3 refused interview. Patients were interviewed once after they had been at home for approximately six months. Information was obtained about their experiences since returning home and from whom, if anyone, they had looked for help in the family, neighborhood, or from professional resources. Interviewing began in January 1956 and was completed in March 1957.

A preliminary analysis of the data calls attention to two facts. First, the total number of patients returning to this community was numerically less than had been expected. Secondly, perhaps similar to many communities, staff had anticipated a total post-hospital population composed primarily of psychotics and were
surprised at the large number of patients with an alcoholic or non-psychotic diagnosis. It would seem logical, therefore, that one of the first practical steps in planning a followup program would be to review carefully with the hospital the variety of patients admitted and discharged.

Other significant activities and projects of the Study Center include:

1. A pilot project aimed at trying out brief family-oriented service. The procedure being tested is to offer families a series of three family group therapy conferences after the usual diagnostic evaluation has been completed. The goal in this approach is facilitating communication within the family.

2. A followup study has been initiated of patients seen for diagnostic services only and then referred to other community agencies.

3. A study and evaluation of general clinical procedures has been initiated. The traditional technique of an intake interview followed by a psychiatric diagnostic session, followed by a psychological evaluation, followed by a staff conference will be under review as will be the voluminous dictation, recording and transcription of each step of the diagnostic and treatment process.

4. The Center continues to work on the development of a way of classifying and filing the varied kinds of data about the county in which it works - its social structure and forces, its sub-cultures and neighborhoods, and agencies. A detailed cross-indexed classification was completed in July 1957.

5. The record system project, begun in fiscal year 1952, had as its objective the design of an integrated set of mental health clinic records, including a coding system for IBM cards. After this record-keeping system had been in operation for five years, the Center staff, this year, completely revised all of the recording methods in use after evaluation was made of each item on each form as to its applicability, practicability of completion and usefulness. Together with the Biometrics Branch, Center staff plan to analyze the five years of data accumulated on IBM cards.

**WORK WITH REGIONAL, NATIONAL, AND INTERNATIONAL ORGANIZATIONS**

Continued efforts have been made to develop program relatedness with national and international official and voluntary agencies. This type of relationship is particularly
important in a preventive mental health program. Mental health programs rather uniquely demand the close working relationship of many individuals, groups, and agencies.

The following are some examples of how the Branch has been working with both national and international official and voluntary agencies in further developing mental health services to people: (1) Joint planning was initiated with the U.S. Department of Agriculture in an effort to take advantage of their interest, and ongoing activities related to mental health. This agency has a tremendous potential for preventive mental health, particularly in rural areas. (2) A staff member of the Branch represented the National Institute of Mental Health at the Third Pan American Congress of Social Service in San Juan, Puerto Rico. (3) Regional office staff have participated actively in the deliberations of the National Social Welfare Assembly regional meetings. These meetings cover a wide range of activities including services to the aging, juvenile delinquency, and mental retardation. (4) Two staff members participated in the 1957 National Association for Mental Health Assembly as leaders of workshops on rehabilitation of the mentally ill, and the relationship of the community and the hospital in the care and treatment of the mentally ill. (5) Both regional and central office staff participated in the 1957 National Health Forum which was devoted to mental health. Regional and central office staff were also active in professional organizations such as The American Psychiatric Association, National League for Nursing, American Psychological Association, National Association of Social Workers, etc.

Working relationships with the Office of Vocational Rehabilitation, Children's Bureau, Public Assistance, and the Office of Education have been greatly strengthened through numerous joint activities. For example, the Branch co-sponsored with the Office of Vocational Rehabilitation a series of regional conferences throughout the United States on the rehabilitation of the mentally ill.

The regional offices concerned (Atlanta, Charlottesville, Dallas, and New York) continue to work with the Southern Regional Program in Mental Health Training and Research of the Southern Regional Education Board, which, with a grant from the National Institute of Mental Health, was successful during the year in employing a mental health staff. Southern Regional Education Board's Council on Psychological Resources in the South has resulted in the first regional program to train school psychologists. Likewise the regional offices in the Western part of the country (Dallas, Denver, San Francisco) continued their work with the Western Interstate Commission on Higher Education to establish a Western Regional Council on Mental Health Training and Research, which received during the year a grant from National Institute of Mental Health to establish, operate and staff the
above council. The New York Regional Office continued its cooperative work with the Northeast States Governments Conference on Mental Health.

As in previous years, many of the regional offices had a meeting of the State program staff in their regions generally to exchange information and experience about program problems and developments. In Region V a regional meeting was held which was focussed on the single subject of mental health education.

COMMUNITY SERVICES COMMITTEE

Recruitment and training of community mental health staff were the major subjects discussed in the two day meeting in March 1957 of the Community Services Committee of the National Advisory Mental Health Council. The Committee discussion was centered about the problem of: (a) how to increase the supply of persons enrolled in professional schools, and (b) how the people in the training centers could be channeled into community mental health programs.

Among the suggestions made were the following: (1) A more intensive, aggressive, and better organized recruitment program is needed, beginning with the high school student, (2) If part of the medical residency took place in a community agency rather than in a hospital, the interest of students in entering community services might be stimulated, (3) A study was proposed to determine the motivational factors which lead an individual to select either private practice, work in a mental hospital or in community mental health services. (4) Community work needs to be made more attractive through such devices as career plans, inservice training, providing maximum responsibility and professional freedom to staff. (5) Special project funds are needed to encourage State hospitals to orient themselves community-wise. (6) Mental health associations should be encouraged to emphasize preventive services and community mental health programs as well as the mental hospital programs. (7) Increased utilization should be made of public health nurses in community mental health programs.

In addition, the Committee took formal action in unanimously approving the recommendation made at the 1956 conference of the State and Territorial Mental Health Authorities that the National Institute of Mental Health provide courses of instruction for orientation of State-level staff on community mental health programs.
Preceeding the formal Conference of the Surgeon General with the State and Territorial Mental Health Authorities, the second annual two-day "Technical Session" was held for community mental health program directors. These informal meetings provide an opportunity for program directors from all parts of the country to exchange information and experiences about program developments and activities. The manpower problem - recruitment, in-service training, retention of staff - was the major subject discussed in the meetings but other subjects discussed included research, State-level program planning and regional programs for sparsely settled areas.

At the formal Conference on November 5, 1957, the Mental Health Authorities passed thirteen recommendations. Three of the recommendations were concerned with training. The first asked for Public Health Service grants of training funds on a matching basis to the Mental Health Authorities to support interstate training centers for professional training in mental health. The second encouraged the training of more personnel for community mental health programs by providing more funds for training grants to operating agencies that are carrying on community mental health programs. The third asked for liberal stipends to general practitioners and non-psychiatric specialists for periods of three to six months of intensive training in mental health.

Two recommendations requested increased Federal grant-in-aid funds for community mental health services. Surprisingly, these recommendations were submitted by New York and California, both large, high-income States that contribute more in taxes than they get back from a Federal grant.

Two recommendations were concerned with meetings of mental health staff. One asked the National Institute of Mental Health to set up a series of regional conferences for State mental health staff and the second asked for a continuation of the annual meetings of community mental health program directors usually held in conjunction with the annual Conference of the State and Territorial Mental Health Authorities with the Surgeon General.

Additional recommendations requested that (a) Hill-Burton funds be extended for use in the construction and equipping of mental health facilities established for cooperative use by several States, (b) the Public Health Service explore with the National Association of Mental Health possible plans for providing orientation for executive secretaries of State mental health associations on the Federal and State community mental health programs, (c) a study be conducted of the present structure of mental health clinics, (d) exploration be made of the possibility of notifying the mental health authorities of Federal grants in the mental
health field made by agencies other than the Public Health Service, in the Department of Health, Education, and Welfare, (e) the Public Health Service prepare and publish a monthly Mental Health Digest. As a recommendation to themselves, the Conference endorsed the principle of establishing after-care programs for released mental hospital patients.
Community Services Branch

BUDGET SHEET

Estimated Obligations for FY 1958

Total: $1,367,667

Direct: $1,314,600

Reimbursements: $53,067
The Professional Services Branch continued to fulfill its function in the fields of program planning, program development, the administration of special grants, budget review, specialized assignments with respect to program problems faced by the Institute, and the provision of consultation within the Institute to other governmental and non-governmental groups.

The major activity of the Branch continues to be research and development in program areas and problems. Special grants are used in this connection to extend, temporarily, the facilities of the Institute. Analysis of the state of knowledge and programs of action, consultation with other groups or agencies concerned with the same problem, and feedback of new knowledge and understandings, especially to State mental health programs, also constitute important parts of this activity. These areas form an over-all pattern, as indicated in the outline and summaries which follow.

Studies Concerned with the Prevention or Reduction of Disability in Pathologic or Deviant Populations

Rehabilitation

Progress continues on two large-scale studies of psychiatric rehabilitation and a third project has been initiated. The Boston State Hospital Pilot Study of Rehabilitation and Rehabilitation Personnel is in the final stage of analysis of data. Dr. Ralph Notman, Principal Investigator, and Dr. Richard H. Williams of the Professional Services Branch, are assuming joint responsibility for preparation of a major report to be published in book form. The study of the post-hospital experience of mental patients is currently in full operation with four more years of committed support. Dr. Ozzie Simmons and his staff at the Harvard School of Public Health have published several papers based on the study. A study of the adjustment patterns of married patients admitted to a mental hospital for the first time, during hospitalization and the post-hospital period, has been initiated in the Department of Mental Hygiene in California. Drs. John Clausen, Morton Kramer and Williams are acting as liaison.

Feedback activities from the rehabilitation studies have increased markedly during the past year. Drs. Notman, Simmons and Williams have consulted with the staffs of several State hospitals and State mental health programs and have participated in regional conferences on psychiatric rehabilitation sponsored jointly by the OVR and the NIMH. A book has appeared, The Patient and the Mental Hospital (Milton Greenblatt, M.D., Daniel J. Levinson, Ph.D., and Richard H. Williams, Ph.D., Editors), which summarizes current research on the social and psychological aspects of treatment and rehabilitation. Dr. Williams is serving as Chairman of an Advisory Committee at the
Massachusetts Mental Health Center (Boston Psychopathic Hospital) which is concerned with a group of studies on rehabilitation, alternatives to hospitalization and the relation between drug and milieu therapies. He also serves on a Panel on Patterns of Patient Care, for the Joint Commission on Mental Illness and Health, and prepared an analytical summary of the deliberations of this group.

**Mental Retardation**

Concern for the mentally retarded throughout the country has been greater during the past year than previously. The amount of research and program development has increased markedly with much improvement of both the quality and quantity.

Activities within the NIMH staff and special grants made in this area have played an important stimulating role.

The American Association for Mental Deficiency project on Technical Planning in Mental Retardation has been working on many problem areas. The primary ones this past year have been: reorganization of the *American Journal of Mental Deficiency*; development of an abstracting service which has been appearing regularly in the *Journal*; publication of review articles (the NIMH supported survey of the etiology of mental retardation done by Drs. Masland, Satason and Gladwin will be published in the spring of 1958). Dr. Leonard J. Duhl is serving as the Associate Editor for Medicine for the *Journal*.

Conferences have been held with medical school deans and heads of the departments of psychology and psychiatry to discuss the inclusion of teaching of mental retardation in medical schools. It is believed that it should be incorporated along with the general program of child development, rather than as a special entity and specialty.

A basic revision of the presently existing nomenclature is in process. This nomenclature will fit the standard American Medical Association version. The revision is being made in cooperation with the American Psychiatric Association committee, the NINDB as well as other Government organizations.

Institution-university cooperation studies are being made to determine how to improve the working relationships between these two groups. Institutions offer a wealth of subjects for research purposes; the universities can both actively participate in research and offer much to improve the institution.

The grant to the National Association for Retarded Children on the etiology of mental retardation is being prepared for publication. One version will appear in the *Genetic Psychology Monographs* and the other in the *American Medical Association Journal of the Diseases of*
Children. They are both being reprinted in the American Journal of Mental Deficiency and will subsequently be circulated by NARC and various Government agencies. This survey has already had a marked impact on researchers.

The third special grant in this field to the Pacific State Hospital, to study the factors involved in institutionalization of the mentally retarded, has begun. In addition to doing cohort studies of the population, attempts will be made to develop measures of individual change. This grant has also allowed for the development of the Pacific State Hospital as a center for research in mental retardation. Major cooperative relationships have developed with University of California at Los Angeles, California Institute of Technology and the University of Southern California. Various departments such as bio-statistics, public health, psychology, psychiatry and chemistry have become involved. Various groups of graduate students have been brought into the program. In addition, many persons not previously interested have been attracted both to the hospital and to work with the retarded themselves. This project ably demonstrates how effects of a research project can spread beyond the research itself.

Cooperation has continued with other agencies in Government, especially the Office of Education. Dr. Duhl has continued to consult on mental retardation, and served as a member of the Office of Education's Research Advisory Board. The Research Advisory Board is responsible for evaluation of research projects in education and has given special emphasis to mental retardation.

**Drug Addiction**

A major study of drug addiction among minors at New York University is in its terminal year of support. Much has been learned about the circumstances under which young people become drug users, the way they are initiated, and the kind of people they are. There has been basic clarification of the delinquency-drug use relationship. We now know the social psychology of drug addiction quite well, even though we cannot control all contributive forces in this field, as we cannot in other problem areas.

There is still concern about this field. The Professional Services Branch is currently exploring the possibility of developing: (1) a sophisticated document on the measures necessary, in terms of community action, to reduce and control addiction and, (2) a small-scale demonstration effort, aimed at the reduction of drug addiction in a part of a large city, with another part of the same city used as a control area. Such a formulation, based upon the research done in the last six years, plus a demonstration, could well lead to similar efforts, on a large scale, with local and/or State financing. It is now felt that basic social science research should be followed by action research.
Juvenile Delinquency

Three special grant projects in delinquency research have been under way during 1957, with Dr. Raymond Gould as the Branch liaison person. The first, at the Thom Clinic in Boston, involves an intensive diagnostic study of hyperaggressive, uncontrollable boys and their families as preparatory to a larger study which is to include both intensive diagnostic study and intensive investigation of the treatment process over a period of several years. The special grant covered the pilot phase of the project, with the understanding that the investigators would apply for a regular grant for the next phase. The application for the regular grant was approved in June of 1957 and the investigators are moving into this phase of the study in December of 1957. At the same time they are completing the analysis and the reporting of the pilot phase. The project is already supplying methodological innovations in the content analysis of interview materials and a deepened understanding of the dynamics of the problem of the hyperaggressive child and his family, with valuable clues regarding effective treatment.

The second project, at the South Shore Guidance Center in Quincy, Massachusetts, has concentrated in its pilot phase on developing a typology of a sample of 50 delinquents who came to the juvenile court in 1957. The typology is designed so as to be relevant for treatment purposes. A first draft of the analysis of the pilot phase has just been submitted to NIMH. The study has included the design of an extensive schedule for accomplishing the social and psychiatric diagnostic study and has involved reliability checks on the observations of the psychiatrist by one or more other psychiatrists. It has also included a specification of the ideal treatment, the recommended treatment, and the actual treatment or disposition prescribed by the court, with predictions regarding the probability of recidivism in each instance. This group is planning to apply for a continuation grant of several years' duration early in January 1958. This project will involve enlarging the sample so as to permit more refined analysis and a program of intensive treatment where appropriate, and intensive follow-up of the sample so as to test the predictions and deepen the diagnostic understanding of the cases.

The third project, with Dr. Lippitt and Dr. Withey at the University of Michigan, is in its pilot phase, using a social-psychological approach to develop a clinically meaningful typology of delinquents, with a focus on the social situation of the child as well as on significant attributes of the child and his family. They are also conducting pilot investigations of significant agencies in the community, such as police, juvenile court, social agencies, and schools. Application for an expansion of this project will be submitted in the spring of 1958.
Dr. Gould has been active as a consultant in delinquency research during the year, and has an article on the present state of delinquency control and research in the December 1957 issue of Federal Probation.

Other Areas

Consideration is being given to the promotion of research and development activities in other areas, under this general heading, including alcoholism, sex deviancy, suicide, family disorganization and the problems of gifted children. No actual work has as yet been undertaken in these areas.

Studies of Fundamental Processes Affecting the Mental Health of Populations of Entire Communities (Local, State and National)

Communication of Mental Health Concepts

A major study in this field, at the University of Illinois, has shown what the population thinks about mental health problems, how these beliefs compare with those of the experts, and what is being said about the theory of mental illness in the mass media. The project has terminal support, and is currently addressing itself to experimental studies of change phenomena in this area, as well as to an analysis of the factors determining how mental health information is secured, screened and transformed by the media. The demographic factors are pretty well understood. The final results should be useable tools for those who want to achieve specific mental health education objectives.

Child-Rearing Practices and Beliefs - The Parental Role

The Illinois studies on communication highlighted a specific problem area—education concerning child rearing or rather the factors responsible for parent behavior with respect to their children. There had been many studies of what kinds of problems children showed as a consequence of particular parent behaviors and child-rearing practices. One of the most definitive was an extensive study by Robert Sears at Harvard with regular research grant support. It became increasingly clear, however, that little was known about the total set of factors that determine parent behavior. The interaction of parent personality structure, beliefs, concepts and hypotheses about child development, value structure and goals for the child, sub-cultural influences, etc., had not been explored for all parents and only in a limited way for those who have produced children needing clinical attention. In short, what is the total set of influences that determine parent behavior? Which of the influences are manipulable by non-clinical methods? What is the natural history of parent role development? The emphasis here is on basic understanding of how a role is developed in our culture. The answers should help greatly to deal with the more applied problem of parent education. This study is being supported on a five-year basis starting in April 1957. The principal investigators are Robert Sears and Wilbur Schram at Stanford University.
Aging

Progress continues on the study of Psychological and Sociological Factors in Successful Aging on a special grant to the University of Chicago, being undertaken in Kansas City. Dr. Williams provides the NIMH liaison. Excellent relations have been established with a panel of about 150 persons between the ages of 50 and 70, with all of whom the staff has conducted four intensive interviews to date. A comparative study has been made of a group of people in their 80's.

A special grant to the University of California Institute of Industrial Relations was recently approved to complete a study of social and psychological aspects of retirement, with Dr. Else Frenkel-Brunswik as Principal Investigator. Dr. Williams has effected liaison between this project and the Kansas City study.

Papers have been presented to scientific meetings by members of the staff of the Kansas City study and Dr. Williams prepared a paper for the 4th International Congress of Gerontology. Dr. Williams is currently preparing a chapter on "Changing Status, Roles and Relationships" for the Handbook on Social Gerontology being prepared by the Inter-University Training Project in Social Gerontology, financed jointly by the NIMH and the NIH. Materials will be drawn from the Kansas City and California studies as well as from the multi-disciplinary study being conducted at NIH. Dr. Williams also is maintaining liaison with the Center for Aging Research at NIH.

Community Decision Making

The staff of the Professional Services Branch has felt it would be valuable to make an analysis of factors in decision-making processes which may affect the mental health of communities. Approval was given by the Executive Staff to develop a project in this area, and a proposal was submitted for consideration by the National Advisory Mental Health Council in November. The Council was divided in its opinion of the proposal, and the majority felt that the time was not ripe for the particular proposal presented. It was therefore disapproved. However, it was clear from the discussion that the Council felt research and development in this area would be important, and undoubtedly further explorations of this field will be made.

The Utilization of Space

The Branch has had a continued interest in the physical and social environment as it relates to mental health. An informal group of consultants from varied disciplines has met regularly to discuss this problem. They have, as part of their discussions, aided in the formulation of several projects. An interesting concept has been developed called population potential, which states that a community closer to centers of population density will react quite differently
from communities at some distance from major population densities. Using this concept and the mathematical formulations associated with the preliminary work has shown, that the prevalence of alcoholism, for example, is greater nearer the centers of population potential than in areas distant from it. Work with city planners has led to their ability to utilize a new dimension in consideration of plans being made for communities. Dr. Duhl has been asked to speak at both the City Manager's Association and the American Municipal Association on topics related to mental health. The interest seems to lie less in concern about mental health clinics and facilities and more with problems of the general impact on the promotion of health of a population. The general importance of human ecology is being recognized. It is becoming evident how difficult it is to deal with a specific problem without considering the multiple factors involved in the community.

**Other Areas**

Some consideration has been given to problems of creativity, but no systematic work has yet been started. The Branch also hopes to undertake a basic study of the logistics of mental health services in the future.

**Studies of Fundamental Processes Affecting the Mental Health of Specific Populations in Organizational Settings**

**Mental Health in the School**

The school is repeatedly alleged to be the community structure next to the home that plays a dominant role in determining the mental health, character, and personality structure of children. In spite of this repeated assertion no careful studies have been made of the mental health influences of the schools. Nearly all of the studies to date have dealt with efforts to identify disturbed children in the school at any one moment with little effort to show the school's etiological relationship. These studies have been valuable as ways of showing the treatment problem faced by the school, the community, or the home; but they have not dealt with the day-to-day psychological events of the classroom and school in such a manner as to give a clear understanding of how the school can play a constructive role in the promotion of mental health and prevention of mental illness while maintaining its social mission as a teaching institution.

The thinking that led to the formulation grew out of the considerations over the last two years of an NIMH ad hoc Committee on School Mental Health and of the work in this area of the Professional Services Branch. The basic idea—that the psychological events of the school and classroom can be directly observed and studied—is a new departure in school mental health. The validity of the formulation has been checked with outstanding child psychologists.
The relationship of the events studied to educational and achievement indices must be a matter of concern since the school's socially designated function is education. The primary concern here, however, is with the nature of the psychological events and their relationship to educational outcome. If they are functionally related, the degree to which one set of variables should be manipulated to affect the other becomes a value judgment which is not determined by research but which may be made by those responsible in the light of research findings. In other words, research in this area is not directed toward arriving at value judgments--rather providing a well documented basis for them.

The National Advisory Mental Health Council at its meeting in November approved a grant to the Bank Street College of Education for five years of support to pursue research along these lines.

Preliminary exploration has started to develop a project concerned with mental health in college settings.

Mental Health in Work Groups

In our highly competitive and expanding economy the work situation is particularly important for mental health, both as a source of support and of health as well as a source of pathology in some instances. Dr. Raymond Gould is the Branch liaison with projects in this area. The National Advisory Mental Health Council approved the initiation of program development in this area in June of 1957 and authorized support for a project of Dr. Chris Argyris of the Department of Industrial Administration at Yale University. In this project he proposes to investigate the observation that the needs of the individual worker tend to be in conflict with the needs and policies of the work organization. In this connection he proposes to conceptualize and develop measures for optimum mental health of the worker (involving a constructive comparison between worker needs and organization needs) as opposed to maximum mental health for the worker (in disregard of organizational needs). Argyris has now completed over 60 interviews with management and workers in a silver manufacturing plant and has prepared a statement of his study design which was approved with enthusiasm by an ad hoc advisory group on November 29.

An application from Drs. French, Kahn, and Mann at the University of Michigan was approved at the November meeting of the National Advisory Mental Health Council. In this project the investigators propose to develop their theory of the dynamics of work organizations, with a more intensive focus on the mental health aspects of these dynamics. They expect to be assisted in this research by Dr. A. T. M. Wilson, industrial psychiatrist of the Tavistock Clinic in England. This developmental phase is to be followed by the submission of applications for specific projects to test hypotheses related to the theory.
Studies of the Mental Health Aspects of Traumatic or Stressful Events in Various Populations

Disasters

The Institute's interest in disasters grew out of early (1949) inquiry by the FCDA concerning the management of populations in event of attack. The Professional Services Branch staff prepared extensive documents on this subject at that time. Later the NRC Committee on Disaster Studies asked for support of some of its work by the Institute. Since it was felt that behavior under extreme circumstances is related to personality and mental health status, the Council made a grant for the partial support of their work. Recently (1957) this grant was renewed. There has been serious consideration of staff representation in the disaster and extreme circumstance area as part of the Community Research Facility Plans.

Epidemics

There has been no real program development work in the epidemic field. The PHS was requested in the summer of 1957 by the Army Chemical Corps to make a study, primarily of industrial reaction, of the impact of the anticipated Asian influenza epidemic. The Service felt that any study made should not be limited to industrial production offices but should encompass as many aspects of community reaction as possible. The participation of the NiMH was requested. Several staff members participated in the planning of the over-all study which is being administered by the Behavioral Studies Section, Public Health Education Branch, BSS. Field studies in selected communities before, during, and after the epidemic period are being conducted. Various aspects of community planning and reaction to the epidemic at various stages are being measured. The NiMH is helping in three ways: (1) Personal services funds equal to one man year at the GS-11 have been transferred to the study to help with field work and data analysis of temporary employees; (2) One social scientist is on detail to the project; (3) A grant was made to support the field interviewing work by National Analysts, Inc. The work in this area has had to be done quickly and without a large amount of preliminary study. It is congruent with the Institute's interest in reaction of populations to conditions of threat.

Urban Relocation

A study has recently begun of the impact of urban renewal and relocation in relation to slum clearance, under the direction of Dr. Erich Lindemann at Harvard. This study, like all studies of human behavior under stress, should highlight some of the mental and emotional components of ecological and social change generally.

Accident Prevention

The Department, and PHS became highly interested in accident prevention in early 1956. NiMH participation in the program of the Service was requested. One PSB staff member was assigned responsibility in this
area. The Service has centered its Accident Prevention Program in the Division of Special Health Services, BSS. The Institute is supplying one staff member to the Accident Prevention Program, Dr. Bernard Fox, a psychologist specifically recruited for the work and technically a member of the PSB. A special grant has also been developed to support a forthcoming conference on research on accident prevention with emphasis upon the possible contribution of the behavioral and social sciences. Regular research grant support of accident prevention studies by NIMH and other parts of the NIH has been encouraged. There is currently some concern being expressed over the basic relevance of some kinds of accident prevention research to the NIMH program.

**Establishment of Research Settings**

Carefully established and planned research settings for studies of human populations, in which basic demographic data are well known and samples of the population may be systematically drawn, can facilitate a variety of studies of special problem areas. Also, results can more readily be made cumulative, and the interrelations of problems more thoroughly understood.

The Community Research Facility Plans, which the NIMH have been developing, would be of much value in relation to most, if not all, of the specific areas discussed above.

The California State Department of Health is interested in the establishment of a "community population laboratory" in the Oakland bay area. It is possible that the NIMH will wish to assist in the effort, in collaboration with other Institutes, and to utilize this laboratory for special studies in the fields of aging, alcohol, and possibly others.

**Conclusions**

All of these areas are being approached from the general perspective of operations research. There is another, and more fundamental element which they have in common. All of them are tending to broaden the basic conceptions of public mental health by analysis of the interpersonal and societal matrices within which each problem occurs. An understanding of these matrices is proving to be basic both to an understanding of the nature of the problem and to the development of methods for its solution.
Several of the studies are explicitly concerned with alterations in social circumstances which go far to overcome other deficits, including deficits of a physiological nature. There is a growing body of evidence that this approach to problems of mental illness and health is both feasible and highly worthwhile.

One of the major efforts in future years should be to consolidate gains made to date, and to explore the interrelated and cumulative aspects of the findings as they are made. It is to be suggested, as a major recommendation, that new areas not be explored at the expense of following through on work already begun.
NATIONAL INSTITUTE OF MENTAL HEALTH

Professional Services Branch

BUDGET SHEET

Estimated Obligations for FY 1958

Total: $157,055

Direct: $150,961

Reimbursements: $6,094

Project included: Community Study Project
During calendar year 1957, more than during previous years, the information and public education activities of NIMH's P & R were weighted in the direction of interpreting and presenting the findings of fundamental research in the basic medical sciences that contribute to the field of mental health. A majority of the major radio and TV programs and magazine and newspaper articles which P & R prepared, or otherwise cooperated and participated in, were on mental health research subjects rather than on needs and services or interpretation of basic mental health subject-matter. The same trend was noticeable in some of the special events sponsored by P & R during 1957 and in consultative and other types of assistance provided to other branches of the Institute and to outside organizations during the year.

In part, this trend was a reflection of the Institute's generally increased research programs, particularly intramurally, as well as of NIH's intensified concentration on research accomplishments, as evidenced by the almost exclusively research character of the weekly report and the call for special reports dealing with various phases of research developments. As a consequence, there have been more demands on P & R staff for studying and keeping abreast of research developments in a wide spectrum of technical areas, and of actively seeking out new developments in the course of preparing articles, reports, speeches, and responses to inquiries. To meet these demands as well as increasing demands on the Director for professional and lay presentations on mental health research, P & R has had the responsibility not only for handling this material accurately and comprehensively but also for presenting it with a keen eye to the broad policies, as well as the public relations problems that might be involved.

In part the trend during 1957 was a conscious effort on the part of P & R to stress mental health research increasingly during the past year or two. Work done during past years, and the increasingly effective activities of the mental health voluntary, have awakened public interest in, and understanding of, mental health problems to the point where the Institute no longer needs to devote major effort to stimulate inclusion of mental health material in the mass media. The major task now is to direct and channelize existing interest and to stimulate attention to neglected areas. This P & R has attempted to do during 1957.

Another important trend in P & R's activities was the greatly increased number of special jobs and special events performed and sponsored by P & R in a partnership role (rather than in an assisting or independent role) with other branches of the Institute. The over-all number of such special jobs greatly increased during 1957. So did the amount of consultation to and work with outside organizations. Some of this special work was done on request. Much of it was actively solicited and performed by P & R in recognition of the essential role of public information and education in the over-all goals and objectives of the Institute and its program.
Work in Special Subject Areas

A large part of NIMH's activity during 1957 was devoted to such key areas as psychopharmacology, aging, mental retardation, and rehabilitation of the mentally ill. Much of the work done by P & R, as an integral part of over-all Institute work, can be described most conveniently under such subject headings.

Psychopharmacology

All of the mass media and the general public were intensely concerned with the tranquilizers, the energizers, and other phases of psychopharmacology during 1957. The year had scarcely opened before NIMH was barraged by press and magazine inquiries stimulated by unfavorable publicity about the Institute's psychopharmacology program. P & R spent considerable time in handling these inquiries, preparing special reports, and otherwise counteracting the adverse results of a public attack on the Institute's program in this field.

To help counteract the effects of this publicity, and to withdraw the Institute from the strategically poor defensive position in which it had been placed, P & R arranged with Jules Billard for placement of a major and authoritative positive statement of NIMH's position on psychopharmacological agents. This appeared as the lead interview-article by the Director in the June 21, 1957 issue of U. S. NEWS AND WORLD REPORT. The article, entitled What You Ought To Know About Tranquilizers, met with immediate and unqualified approval by the psychiatric profession, the medical profession, special interest groups, and the general public, and the Institute was uniformly congratulated on its firm stand in the field of psychopharmacology. U. S. NEWS AND WORLD REPORT generously supplied several thousand reprints to satisfy requests for copies of the article received from all parts of the country. It is of interest that Dr. Allman, President of the American Medical Association, quoted from the U. S. NEWS piece in his article on tranquilizers that appeared in AMERICAN WEEKLY late in 1957.

Another major article on The Tranquilizer Question was a piece with that title by Frank Bello in the May 1957 FORTUNE magazine. Based in large part on information supplied by the Institute's Psychopharmacology Service Center, through arrangements made by P & R, this was a comprehensive article on the subject of psychopharmacology. P & R made arrangements to procure reprints and has been using this piece, along with the U. S. NEWS piece, as a regular part of its informational materials.

A number of important press articles on psychopharmacology, prepared with assistance from P & R, appeared during 1957. The more important of these included several articles in a series on mental health by Howard Whitman in the COLE NEWSPAPER SYNDICATE, several by Selig Greenberg in his series on New Horizons in Medicine in the PROVIDENCE JOURNAL-BULLETIN, a SCOPE piece on the NIMH program of clinical research on anti-depressive drugs, a NEW YORK TIMES piece on tranquilizers by John Finney, and a lead article on the Psychopharmacology Service Center in SCOPE WEEKLY. In addition, information on psychopharmacology was provided to writers from the AAA magazine, REPORTER, CHEMICAL AND ENGINEERING NEWS, PHYSICIANS MAGAZINE, READERS DIGEST, CAPITOL TIMES, WASHINGTON POST, GANNETT NEWSPAPERS, N. Y. DAILY NEWS, WORLD-WIDE NEWS, NEA SYNDICATE, NEWARK EVENING NEWS, SCIENCE SERVICE, and INS.
Three major TV shows, in which P & R had an important role in selecting topics and making arrangements, were devoted to psychopharmacology. One, the American Association for the Advancement of Science hour-long NEW FRONTIER program, appeared on the CBS-TV Network at the very close of 1956; the Chief of NIMH's Psychopharmacology Service Center was guest panelist on the section of the program dealing with the biological sciences. Arrangements were made for the Chief of the Center to give a medical exposition of tranquilizers on Howard Whitman's special half-hour program on tranquilizers produced as part of a national hook-up NBC-TV HOME show. Toward the end of the year arrangements were again made for Dr. Cole to appear on TV — this time the McCaffrey CELEBRITY PARADE (WMAL-TV) in a discussion of tranquilizers and tensions.

In addition, P & R provided information and arranged for consultation to an independent film maker who is currently preparing a medical film on tranquilizers addressed to the general physician, and assisted Editorial Research Associates on their new pamphlet on psychopharmacology. During the year, the Chief of P & R served as a member of the Committee of Editors in a Working Conference on the Status and Improvement of Clinical Drug Evaluation Reports sponsored jointly by the Institute's Psychopharmacology Service Center and the American Psychiatric Association.

Gerontology Conference

P & R's major activity in the field of aging for 1957 was complete coverage and handling of the press relations and publicity program for the Tenth Annual Scientific Meeting of the Gerontological Society held in Cleveland on October 31 - November 2, 1957. Carried out by P & R staff at the request of the Chief of NIMH's Section on Aging, who was Program Chairman for the meeting, this was a highly successful and extremely important undertaking which increased P & R's prestige with NIMH and outside scientists in the field of aging, as well as NIMH prestige for its leadership in this field. Preliminary to the meeting, contact was made with and publicity materials distributed to 22 editors of metropolitan newspapers with large national circulations, 22 selected science writers with a known interest in gerontology, program managers of all the principal radio and TV stations in Cleveland, and the CBS, NBC, and WESTINGHOUSE radio and TV Public Service departments. Two advance press releases, one a general announcement and the other on a special symposium of European gerontologists, were sent to 200 large dailies plus some professional journals. The N.Y. TIMES, the N.Y. JOURNAL-AMERICAN, and AP sent reporters from headquarters; INS and UP were covered by the Cleveland bureaus. In addition, requests for all releases and papers were received from SCIENCE SERVICE; Roland Berg, Medical Editor of LOOK; the Managing Editor of MEDICAL NEWS; Earl Ubell of the N.Y. HERALD-TRIBUNE; Tom Henry of the WASHINGTON STAR; the editor of the PITTSBURGH SUN-TELEGRAM; Robert P. Goldman of PARADE; Ray Bruner, Science Editor of the TOLEDO BLADE; free-lance writers; Richard C. Bostwick of SMITH, KLINE and FRENCH; and Fred Freed of CBS.

As part of the press coverage, condensations of the major papers to be delivered at the Conference were prepared and these were made available at the press room, along with suggested leads, biographical sketches of the principal speakers, photographs, and printed programs. P & R staff members were in Cleveland for the meeting, set up the press room, and took care of all public relations for the Conference. Three days ahead of the
meeting a staff member went out to do advance publicity with the managing editors of the three Cleveland papers, the three wire services, and the two radio stations and one TV station which had expressed interest in interview programs with gerontologists attending the meeting. In addition, P & R had an NIMH exhibit at the Gerontology meeting.

Immediate results of P & R's publicity work at the Gerontology Conference included:
1) Two radio interviews with gerontologists on Cleveland's WGAR and KYW.
2) One TV interview with Dr. Bourliere of France on WJW.
3) Advance stories in N.Y. TIMES and other papers.
4) Daily stories in N.Y. TIMES and over AP and INS. AP stories were carried on front pages from N.Y. HERALD TRIBUNE to SEATTLE TIMES, from Great Falls (Mont.) LEADER to Louisville (Ky.) TIMES, from Ithaca (N.Y.) JOURNAL to Idaho Falls POST-REGISTER, and many others, both large and small. INS coverage was also widespread.
5) Daily stories by medical writers in CLEVELAND PLAIN DEALER, and daily feature stories with pictures in CLEVELAND PRESS. Also publicity in CLEVELAND NEWS.
6) Round-up article by WORLD WIDE NEWS in November 20 issue of SCOPE WEEKLY.

In addition to these immediate results, various feature articles will no doubt result from this public relations work. Two of the reporters who covered the meetings write columns related to gerontology, and many of the free-lance and magazine writers who requested materials will probably use them as source data for future articles.

Other Work on Aging

Mental Health of the Elderly, a new pamphlet prepared by P & R, was issued describing NIMH's varied activities in the field of aging. It was also translated into French and Italian, and copies (including those in English) were sent to Italy for display and distribution at the International Gerontology meeting. GPO has reported relatively high sales of this pamphlet (a total of 1500 being sold in the 3 months from June to September), and a second edition was run off in 1957.

As part of its assistance in the press room at the annual meeting of the American Psychiatric Association in May, P & R staff prepared press announcements on papers delivered by NIMH personnel on their research in aging, and arranged for a press conference with two of these scientists. This activity resulted in a number of press articles on NIMH research on aging and mention of this work on 3 network radio programs. Several months after the meeting, P & R wrote an article on the research work of one of these scientists for Tom Henry in the WASHINGTON STAR. During the year, information on aging was also given to Fishbein of WORLD-WIDE NEWS, to Beach of U.S. NEWS AND WORLD REPORT, and to Cassels of UP.
Another major informational event in the field of aging was the Johns Hopkins FILE 7 TV show, in the fall of 1957, devoted to the sociological and psychological aspects of aging, with the Chief of NIMH's Section on Aging as guest speaker. P & R worked with the script writer and helped make arrangements for this program.

Mental Retardation

During the year, P & R was called upon to assist in revitalizing the JOURNAL ON MENTAL DEFICIENCY, published by the American Association of Mental Deficiency, the principal professional organization in the field of mental retardation. At the request of a member of NIMH's Professional Services Branch who had become Medical Editor of the JOURNAL, a P & R staff member was assigned to develop magazine policy, to set standards for manuscripts, to develop editorial guidelines and procedures, and to get the JOURNAL operating on a journalistically professional basis. A major policy statement, prepared by this P & R staff member, was adopted by the JOURNAL, as were the editorial guidelines. She also edited a number of highly technical professional articles in order to provide the Medical Editor and other JOURNAL staff with prototypes and practical guides.

At the close of the year, P & R worked closely with the National Association for Retarded Children, the principal voluntary in this field, in preparing releases and other advance publicity as well as in making arrangements for a special meeting and press conference (held in New York City in January 1958) in connection with release of two major reports on research on mental retardation, prepared under the sponsorship of NARC with the aid of a grant from NIMH and NINDB. Firm relations were established with the information, publicity and executive directors of NARC, and P & R plans to work closely with that organization in planning appropriate joint activities.

During 1957, WGAY, a local radio station, carried a taped interview on retardation with the Professional Services Branch specialist on this subject. P & R also prepared a number of speech materials for top level speakers on retardation during the year, and assisted a writer from the N.Y. DAILY NEWS with a story on patients in hospitals for the mentally deficient.

Mental Health of Children

P & R prepared three speeches dealing with mental health of children during 1957, one for the Director of NIMH on Services and Programs for Mothers and Children (delivered at the annual American Public Health Association meeting in Cleveland), and two for the NIH specialist on school mental health (delivered at the National Education Association Centennial Convention and Syracuse University's Second Annual Conference on Secondary Education). P & R is assisting this school mental health specialist on a regular basis, collecting pertinent research data for his use, evaluating the usefulness of such material, and advising him of its potentialities for articles in various types of outlets. P & R will prepare some of these articles and provide editorial assistance on all of them.

P & R prepared a statement for and assisted in an open house, held by NIMH's Residential Treatment Center for emotionally disturbed children, for members of Montgomery County citizens' associations. Also coincident with
the opening of the Center, a series of still pictures showing normal controls were taken for subsequent public relations and other informational uses. Some of these pictures were used for an INS story. MEDICAL NEWS carried a major picture story on the Treatment Center and the January 1958 issue of HARPER'S carried an excellent major article on the work of NIMH's Child Research Branch; P & R assisted with both of these articles. In addition, information was provided to LOOK for a major article on emotionally disturbed children, and to Eve Edstrom of the WASHINGTON POST on treatment facilities for such children.

Arrangements were made for NIMH's Chief of the Section on Child Development to discuss IQ testing on ABC-TV's OPEN HEARING, a Network program. P & R wrote 3 articles in collaboration with this Section Chief: (1) a guest column on IQ testing for Jane Eads AP column, (2) a 3,000 word story on adopted children for CHILDREN magazine, and (3) an article on predicting children's intelligence for the NATIONAL PARENT-TEACHER magazine. Information on IQ testing was also provided for a WASHINGTON DAILY NEWS story.

P & R helped with arrangements for an article on normal children in the February 1957 issue of BETTER HOMES AND GARDENS, and for a prospective article on child rearing being prepared by a free-lance writer. In addition, a statement was prepared for the Director's signature on the new PIERRE THE PELICAN series of child-rearing leaflets for parents, produced by the Louisiana Mental Health Association.

A number of the large meetings at which P & R exhibited and displayed materials during 1957 were held by organizations directly interested in or vitally concerned with the mental health of children. These included the biennial meeting of the American Association of School Administrators (17,000 registered attendants), the American Orthopsychiatric Association annual meeting (5,000), the 12th Annual Conference of the Association for Supervision and Curriculum Development of the National Education Association (3,000), the American Academy of Pediatrics (1,000), the NEA annual convention (20,000), and the New York Congress of Parents and Teachers (7,000).

Treatment and Rehabilitation of the Mentally Ill

As part of its emphasis on rehabilitation of mental patients during Mental Health Week in 1957, P & R prepared a 4-minute 15-second tape recording of the Director of the Institute on the subject of The Healing Community, dealing with the role of the community in helping the former mental patient make a successful adjustment. P & R offered to transcribe this talk onto blank tapes sent in by any individual or organization. Though the tape was not available until shortly before the Week, some 20 requests for the tape were received from radio stations and mental health associations. It is planned to continue this type of activity, with promotional assistance from the National Association for Mental Health and the Mental Health Materials Center.

In this same general area, P & R prepared an outline for a speech given by the Director at an APA Mental Hospital Administration session, and drafted a progress report on NIMH's program of Mental Health Projects
Grants, which are awarded for studies and demonstrations of improved methods of patient treatment and care.

Information was provided to the NBC-TV Public Affairs Department for a documentary on mental hospitals, and to Howard Whitman for a half-hour program on rehabilitation on the NBC-TV HOME show. Writers for TIME, READERS DIGEST, COSMOPOLITAN, and INS were helped with stories on day-and-night-care programs, rehabilitation of the mentally ill, identifying and receiving help for the emotionally disturbed, commitment procedures, and resident patient populations.

Research

Research, both intramural and extramural, was emphasized wherever appropriate in P & R's work during 1957. The research interest is apparent in many of the activities already described, and will be integrated into the discussion of activities in subsequent sections of this report. This section describes some of the more important P & R projects which are of primary relevance to basic research and which do not lend themselves to treatment under special subject headings.

Starting in July, the Institute Director's Weekly Report, prepared by P & R, was heavily weighted in the direction of research. In the preparation of research items for these reports, P & R has received excellent cooperation from NIH's research programs; a staff member has been invited by the Director of Basic Research to sit in on staff meetings. In all, 75 items were included in NIH's weekly reports to NIH from July 1 to December 31, 1957; of these, 53, or more than two-thirds, were incorporated into the NIH reports to the Surgeon General. This material proved to be extremely helpful in preparation of Research Highlights of 1957 which, as in past years, was prepared by P & R.

P & R prepared a number of releases and research papers delivered by NIH staff at professional meetings, wrote a speech for the Director on Current Trends in Psychiatric Research for a Regional Research Conference of the American Psychiatric Association, and assisted the American Psychological Association in planning a press reception for a foreign world-renowned neurophysiologist.

During 1957 the script for the proposed NIH film on Mental Health Research was completed and the project approved for production. The film was planned as a public relations tool to acquaint the general public with the nature and scope of mental health research, and thereby to help dispel some of the prejudices against psychiatry and the field of mental health, as well as to help relieve some of the ingrained pessimism about the ability to treat mental illness successfully.

P & R arranged for an NIH researcher to discuss the physical effects of emotions on the ASK-IT-BASKET WTOP-TV program, and for the Director to discuss mental health research in the SCIENCE SERVICE series of taped radio programs. NBC-TV was given information for a documentary on stress.

In addition to research articles mentioned in other parts of this report, P & R assisted in arrangements and information for the 4-article series on alcoholism written by Cassels for UP. Information on research grants and intramural research projects was provided to free-lance writers and writers from MODERN MEDICINE, TIME, LIFE, READERS DIGEST, SCOPE, PAGEANT,
Work With Voluntaries and Other Organizations

As in past years, P & R worked very closely with the National Association for Mental Health in planning and carrying out public information and education programs, both in connection with Mental Health Week and in connection with year-round activities. In addition, assistance and consultation were provided to an increasingly larger number of other organizations, such as State and local mental health associations, voluntary and professional associations in the field of mental retardation, and a wide variety of civic, service, and quasi-governmental groups with a primary or ancillary interest in, and concern with, problems of mental health and mental illness.

Mental Health Week

During the first week in May, NIMH and NAMI jointly sponsored the 9th annual celebration of Mental Health Week. With the theme "The Mentally Ill Can Come Back," the Week was focused on what citizens and communities can do to promote the full recovery and rehabilitation of the ex-mental patient. During 1957, the Advertising Council again ran messages supporting celebration of the Week in the May-June issue of their RADIO-TV BULLETIN.

P & R prepared special Mental Health Week kits, each containing a careful selection of program, publicity, information, and educational materials to be used in celebrating Mental Health Week and in planning long-range mental health activities. These kits were mailed out to some 600 mental health voluntaries, civic and service organizations, mental health agencies, and other interested groups. Selected publicity materials were sent to science writers and others in a position to promote the overall goals of the Week. Included in the kits were a new version of a Mental Health Fact Sheet prepared for the occasion by P & R, and announcements of the tape recording of the Director's talk on The Healing Community. Additional requests for kits and for extra copies of certain materials in the kits were received prior to the Week and subsequently.

The Mental Health Week kit, in the past year or two, has developed into an important program item, apart from its use in connection with the Week. Kits are requested throughout the year by local and State mental health agencies and organizations for use in planning and conducting program activities. As an example, the Bureau of Community Mental Health Services, New Jersey Department of Institutions and Agencies, has requested kits to assist them in developing community mental health education as a first step in setting up the County Mental Health Boards required under the newly enacted Community Mental Health Services Act of the State of New Jersey.

A number of radio and TV programs and magazine and press articles during Mental Health Week were a direct or indirect result of P & R activities. In addition, P & R prepared two speeches for use during Mental Health Week (one delivered by the Director and another by an Assistant Secretary of DHEW), and the Presidential Message and Proclamation for Mental Health Week.
Work With NAMH

NIMH worked with and assisted the Advertising Council and the NAMH in the Advertising Council's major year-round mental health education campaign which was launched in 1957. P & R can claim a good share of the credit for the fact that this campaign was developed, since P & R established the contact with the Ad Council in 1952, built up relations and cooperation with the Ad Council Program Consultant and other staff during the past six years, and assisted in establishing relations between NAMH and the Ad Council. In connection with the Ad Council's distribution of How To Deal With Your Tensions as part of the general mental health campaign, P & R arranged for a foreword by the Director of NIMH, and is assisting in distributing the booklet.

P & R continued its periodic consultation with the public relations and educational directors of NAMH in order to plan joint programs and provide distribution of each other's materials. P & R prepared the message from the President to the Annual Meeting of NAMH. NAMH, in turn, has promoted distribution of two new P & R publications: Facts About Mental Health and Mental Illness, and the Barbiturates leaflet. At the end of the year, P & R was planning joint publication, with NAMH, of a series of leaflets and folding-card exhibits for teen-age audiences describing the work of mental health professional personnel and the kinds of training and experience such people must have. At the end of the year, also, P & R was planning cooperative public relations with a newly appointed special liaison representative of NAMH. Contemplated activities include preparation of a series of charts and leaflets interpreting NIMH activities to State mental health associations, and cooperation with NAMH field representatives and regional groups of mental health organizations.

Work With Other Organizations

During the year, P & R provided consultation to an official of the Southern Regional Education Board engaged in preparation of a special report on the work of that organization. Assistance was given to the General Federation of Women's Clubs on a popular pamphlet being prepared by the Federation on what mental health means to the individual and the family. Consultation and other help was given Editorial Research Associates on their new pamphlet on psychopharmacology.

A speech was written for delivery by a Government official at the Rhode Island State Mental Health Association, greetings were sent for the Director of NIMH to a meeting of the Louisiana Mental Health Association, forewords were written for two pamphlets published by the Westchester (N. Y.) Mental Health Association, assistance and advice were provided an official of the Oregon Mental Health Association, and a series of film previews were arranged for a teachers' workshop conducted by the Washington School of Psychiatry.

Mental health materials prepared by P & R received wide acceptance and use by key organizations. The Canadian Broadcasting Company purchased 8 prints of Preface To A Life for a nationwide telecast. The Bureau of Health Education of the American Medical Association requested copies of a packet of NIMH educational materials for use in their health education program. The Mental Health Materials Center included copies of P & R's
Reference Guide No. 3, Introductory Readings in Mental Health, in their kits which go to 2500 individuals and organizations active in human relations work. Two State Health Departments purchased 15,000 copies of What Is Mental Illness, the popular leaflet prepared by P & R. 6,500 copies of Careers in Psychiatric Social Work and 1,500 copies of Mental Health of the Elderly were sold by the Government Printing Office from June to September 1957, and 3,000 copies of Barbiturates As Addicting Drugs were sold between September and December.

Exhibits and literature displays were sent to meetings of a wide variety of voluntary and other organizations which play a key role in promoting mental health. These organizations included the American Academy of Occupational Medicine, the National League for Nursing, the National Conference of Social Workers, the National Education Association, the American Personnel and Guidance Association, the Cleveland Health Museums, a number of county mental health associations, and the National Health Council. This activity has been a major phase of P & R's public relations and educational work for 1957.

Other Activities

Many of the activities already described--speeches, articles, radio and TV programs, exhibits, special events, and consultations--are directly related to public relations work for NIH as an institution. The press releases, announcements, and answers to public inquiries are also integral to P & R's public relations work for the Institute. In addition to these activities, P & R wrote and provided still pictures for an article entitled Report from NIH which appeared in the October 1957 issue of STATE OF MIND, the monthly magazine published by CIBA for the general practitioner.

P & R staff also assisted a number of the scientists at NIH in organizing, formulating, and presenting their scientific data. In addition to the Weekly Reports and the Research Highlights for 1957, P & R also prepared the Director's Budget Testimony and the short-form annual report, as well as supervising preparation of the long-form annual report.

P & R, at the request of the Chief of the Training Branch, wrote a comprehensive historical analysis of NIH's training programs which is to be included in the Institute's report on training being prepared at the request of Congress.

Recognizing its responsibilities for developing competent personnel in the field of mental health information and public relations, P & R for the first time established a position for, and recruited an Information Trainee. A comprehensive training program, including evaluation, was planned and scheduled with NIH Branch Chiefs, the Office of Research Information of NIH, and the Special Assistant for Information to the Surgeon General. Under supervision, the trainee developed a new system for cataloging and controlling distribution of publications. This system has been put into effect with gratifying results.

The number of public inquiries answered during 1957 was extremely high. An estimated 1800 letters of more than routine difficulty, including about 50 Congressional letters were sent out (based on actual count of 891, including 24 Congressional, from July 1 to December 31). Replies to Congressional letters require knowledge of NIH policy, considerable original research in gathering data for the reply, and a keen sense of
public relations in presenting the material.

Approximately 2,114 telephone inquiries were handled from July to December 1957.

A total of 83,047 pieces of literature were distributed in answer to 8,342 requests during 1957. This was about two and one-half times the volume handled in 1956; the number of separate requests also rose by about 50 percent. Over 300 clearance papers were handled by P & R, and 1133 film bookings were made during 1957.

New Publications and Other Materials

Two new pamphlets and two new leaflets were issued in 1957. One pamphlet, Facts About Mental Health and Mental Illness, was prepared for Mental Health Week and has proved to be so useful that P & R plans to reissue it from year to year, bringing the figures up to date each time. Mental Health of the Elderly, the other pamphlet, was prepared as an extended printed version of the original NIMH exhibit of the same title. This publication, which describes the comprehensive activities of NIMH in the field of aging, was also issued in French and Italian for use at the International Gerontology Congress in Italy.

What Is Mental Illness?, the NIMH leaflet which was distributed in large quantities in its pre-publication edition, was received from GPO early in 1957. Large quantities of this leaflet have been distributed, 15,000 copies being sold by GPO to two State health departments in a single week. The other new leaflet, entitled Barbiturates As Addicting Drugs, has filled an urgent need and met with unqualified approval. The Food and Drug Administration requested 1,000 copies for use in their District Offices, and the GPO, which reported 3,000 copies sold between September and December 1957, went back to press for a second edition of 2,000.

Reference Guides Nos. 1 and 6, Mental Health For Parent and Child and Advanced Readings in Mental Health were revised, as was the Current Reading List of mental health pamphlets, reprints, and reports available from P & R.

Mental Health Memo No. 1, the first issue of a proposed series of digests of significant program activities designed as a means of communication for operating agencies throughout the country, was prepared and sent to some 550 individuals and organizations, including State Mental Health and Mental Hospital Authorities and NIMH regional staff.

Copy was prepared for an abridged statement of Institute functions to be entitled National Institute of Mental Health—A Summary Statement. This will be issued as a leaflet to be sent in response to inquiries from students and others who do not need a fully detailed description of NIMH.

In addition to new NIMH publications, P & R purchased distribution stocks of 29 new reprints during 1957. These covered such varied subjects as narcotics addiction, delinquency, psychiatric terminology, treatment of the mentally ill, family mental health, child guidance,
scientific developments, legal problems in mental illness, tranquilizing drugs, communication of mental health concepts, and mental retardation.

Prints of three new films were purchased during 1957: The Kid Brother, and To Your Health, new films on alcoholism; and The Human Side, a film on volunteer programs in mental hospitals.

The Public Relations of Mental Health Education

The special nature of the mental health field, with its attendant difficulties in communicating information that conflicts with existing attitudes, and the special role of the NIMH as a leader in mental health research, training, and service programs, have posed unique problems for P & R. In meeting its responsibilities, P & R has attempted to develop its information and public relations activities so that they help promote the goals of mental health education. Similarly, educational projects are carefully planned so that they constitute good public relations for mental health in general.

During 1957, P & R was involved in a number of activities intimately related to these public relations aspects of mental health education. The Chief of P & R participated in a panel on mass communications at the National Health Council's National Health Forum (held in Cincinnati in March) which was devoted to the subject of Better Mental Health. The presentation, in addition to being published in the National Health Council's official report of the 1957 National Health Forum, was published as an article entitled Mass Communications and Health in the August 1957 issue of the New Jersey PUBLIC HEALTH NEWS. Copies of this article were procured by the California State Department of Health for distribution to all State health educators, to all health educators in training, to mental health service personnel, and to reference libraries for public health personnel. The spring issue of MENTAL HYGIENE, the professional quarterly published by NAMH, also quoted excerpts from this presentation.

P & R assisted in the preparation and review of the series of five articles on psychiatry and psychology today, carried in LIFE starting with the January 5, 1957 issue. In addition to providing information and materials for the articles, P & R was instrumental in guiding their development and general approach, both through direct review and through communications with the two APA's, who were given major responsibility for review by LIFE.

In May of 1957 the Chief of P & R participated as discussant in a symposium on Public Awareness and Problems in Mental Health at the 12th Annual Conference of Public Opinion Research held in Washington, D. C., by the American Association for Public Opinion Research. P & R also participated in providing consultation to the program director and other officials of the Educational TV Center, Ann Arbor, Michigan, who are planning a series of mental health programs. In addition, P & R participated in consultation with researchers from the University of Illinois Institute of Communications Research who are conducting a special study of communications of mental health concepts under a grant from NIMH.
NATIONAL INSTITUTE OF MENTAL HEALTH

Publications and Reports

BUDGET SHEET

Estimated Obligations for FY 1958

Total: $176,229

Direct: $169,391

Reimbursements: $6,838
RESEARCH GRANTS AND FELLOWSHIPS BRANCH

Annual Report for Calendar Year 1957

The continuing and rapid growth of the research grants program made 1957 a year of significant development and reassessment in Branch operations. Reaffirmation in the fiscal 1958 budget of last year's strong Congressional support for research in mental health, again testified to a steadily growing social concern over problems related to mental ill-health, as well as to an increasing public recognition of research as a vital national resource.

I. PROGRAM GROWTH AND DEVELOPMENT: THE ADMINISTRATIVE PICTURE

Throughout the year the steadily mounting volume of grant applications was to necessitate a series of modifications in program administration. A glance at the following comparative figures on new grant applications furnishes a rough index to the growth of the program. Excluding applications relating to previously committed funds (i.e. continuation and supplement applications), the number of grant applications received has risen from 260 in 1955, to 457 in 1956, and reached 683 in 1957. Numbers of research grant applications which were approved rose from 130 in 1955 to 242 in 1956, reaching 292 in 1957.

Program Administration

It is apparent at a glance that the volume of work necessitated by the review and approval operation has very materially expanded in the last two years. Concurrently, the staff of the Branch has increasingly been called upon to provide advisory and consultative services to grantees, prospective applicants, and to university departments in the behavioral, medical, and biological sciences. Difficulties arising from an acute shortage of staff at the outset of the year were compounded by the loss of staff time in providing repeated and lengthy information statements for budget justification and other administrative purposes. Uncertainty as to 1958 appropriations impeded Branch planning for many months. It
has been difficult for Branch staff members to undertake the necessary degree of stimulation of special areas of research in which the Institute has a primary interest. While it has been a continuing problem this year to meet overall demands for service, members of the staff have been hard pressed as well to find time to keep abreast of recent research developments in the multi-disciplined fields which underlie research in mental health.

A loss of experienced Branch staff was occasioned in April, 1957 with the transfer of the Mental Health Study Section to the Division of Research Grants. So heavy had the task of reviewing the increased volume of research grant applications become that a sister Study Section to the Mental Health Study Section, the new Behavioral Sciences Study Section, was established at this time.

Some of the new staff positions established this year to meet the increase in work-load have been filled - including those of a Program Analyst, a new Executive Secretary of the Mental Health Small Grants Committee, and an Executive Secretary of the Mental Health Career Investigator Selection Committee, together with the new complement of the Psychopharmacology Service Center. Other positions are as yet still vacant. It has proven difficult, as is true in many scientific fields today, to locate well-qualified applicants. Even when qualified people are hired, a long period of training and experience in the Branch is necessary before new staff reach their full work value within the Branch setting. This problem offers no hope of immediate solution.

To help in the training of new staff members brought on during 1957, an orientation series of "discussion-question-answer" sessions have been held at intervals, individual background orientation folders have been prepared, and, through the medium of weekly staff meetings and routine circulation of information materials to all staff members, a strong effort has been made to establish that necessary intercommunication without which few work groups function successfully. Further effort in this area included a major reorganization and consolidation of Branch files to ensure the immediate availability of background information to all staff members.

The growth in the volume of applications for research grants has very markedly increased the number of individual consultations with research investigators. A considerable share of such consultation is conducted by mail, but many personal interviews have been held by the staff in Bethesda as well as at conferences and professional meetings. During 1957, staff members participated in a variety of conferences, including the Conference on Research in Mental Health held in
Jacksonville, Florida, in April, and the Southern Regional Education Board's Conference on Mental Health Research in the South, held in Williamsburg, Virginia in August, 1957; annual and regional meetings of such professional groups as the American Psychiatric Association, American Psychological Association, etc. Branch staff also visited some fifteen to twenty university departments in the biological and behavioral sciences as advisors and consultants on research programs.

Analysis of Program Needs

The judicious distribution of grant funds carries with it some requirement that those responsible for the program work from a sound basis of knowing "where you are, where you are going, and how you can best get there." To acquire such a platform for operating necessitates a continuing program analysis. Increasingly, also, the Branch has been called upon to furnish analytic information on the grants program -- to the Study Sections, the National Advisory Mental Health Council, branches of the Public Health Service, other government agencies and the public. To a greater extent than in the past both the Council and Study Sections have turned to the Branch for information on policy, on program direction and planning.

In an effort to meet both internal and external demands for program analysis, the Branch this year took a number of steps to develop long-range methods of administrative review and critical examination. A part of this new activity has been directed toward the establishment of a sound and workable basis for "categorizing" grants. Since the spring of 1957 a large part of the time of one staff member has been spent in the development of a system of grant analysis, in which defined and standardized processes of content analysis will be combined with mechanical sorting procedures to permit of rapid selection. It is hoped that the successful establishment of the grants category system will facilitate not only the sort of program analysis which concerns itself chiefly with how much research was, or was not, supported (in terms of numbers of applications, amounts of money, distribution by fiscal years, areas of study, etc.), but may later assist in interpreting contributions to scientific knowledge.

Still a further avenue of program analysis was explored by another staff member in a detailed study of the overall role of program evaluation within the Branch, based in large measure on an historical analysis of related earlier experience. This study indicated the need for, and feasibility of, preparing analytic reviews on subject areas of the research grants program, an overall historical review of the administrative development of the program, and additional information articles interpreting the program to scientific audiences.
While lack of staff time this year has limited the preparation of analytic studies, several short reviews of special aspects of the program were undertaken, including a statistical analysis of the research fellowships program, a background paper (for use by the Study Sections and Council) considering fluid funds in the award of research grants, and a more substantial review of the Small Grant Program. With an aim of determining the availability and nature of grant support in mental health and related disciplines from foundations and professional organizations, the Branch this year also has prepared a survey-questionnaire, presently in process of clearance, which will be circulated to some seven hundred private organizations.

The Small Grant Program

The year 1957 also produced a serious review* of the Small Grant Program. Initiated by the National Institutes of Health on an across-the-board basis in March, 1956, the program had been planned as a new method of research support in which the usual deadlines would be waived. Maximum awards under the Small Grant Program are $2,000 plus indirect costs. It was hoped that the program would provide support for such purposes as small-scale pilot studies, modest assistance to young investigators, assistance for minor research needs, etc.

In the late fall of 1957, a general assessment of the Small Grant Program was undertaken in all the National Institutes of Health. While the Program has been less successful in other Institutes, N.I.M.H. has found it to be a workable and desirable means of granting funds in a flexible and rapid manner for certain types of limited research needs.

From September, 1956, to October, 1957, the Mental Health Small Grant Committee reviewed 249 applications and approved 112 -- a 45 per cent approval rate. Almost ninety per cent of the applications approved constituted awards to research investigators who had not had previous support from this Institute. More than half of the approved applications could be classified as "exploratory and pilot studies." Sixty-four per cent of the applicants were psychologists, 13 per cent psychiatrists, with sizable minorities from sociologists and anthropologists.

At its November, 1957 meeting, the National Advisory Mental Health Council endorsed continuation of the Small Grant Program in this Institute at the same level of financial support.

Program Grants and Fluid Funds

The question of how public funds for research may most productively and equitably be distributed is a continuing concern to grant-giving agencies. Since its inception in 1945, the Public Health Service program of research grants has been based on the support of projects and programs. This year, as in earlier years, the query was again raised in the National Advisory Mental Health Council as to whether supplemental support for those research needs which did not fit into the usual research project or program, might be given through lump sum "block grants" to institutions or departments, which could then distribute the funds as they saw fit among departments or investigators.

As a result, the whole subject of fluid funds and program grants was comprehensively aired this year, in committee discussion, administrative consultation, and at the Council and Study Section meetings. In a final review, the Council recommended that increased emphasis continue to be given to the award of long-term program grants to investigators of established competence in the planning and direction of a program of research. Applications for such program support, the Council felt, should be prepared within the context of the present N.I.H. grant program and should be evaluated primarily on the capabilities of the investigator (together with project-site visits to review all such applications) rather than on the detailed specifications of projects to be pursued. The Council suggested that the staff of the National Institute of Mental Health encourage the submission of applications for program grants whenever it is deemed appropriate.

II. THE SUBSTANCE OF THE RESEARCH GRANTS PROGRAM

Underlying the seemingly heterogeneous nature of the basic and applied research supported in the extramural program of the National Institute of Mental Health is a necessarily comprehensive view of the etiology, prevention and treatment of mental illness. While tremendous strides have been taken in twentieth century research in the biological and behavioral sciences, our knowledge of the fundamental processes of men's functioning in his environment is still very fragmentary. Occasionally, a researcher's "serendipity", that original "gift of finding agreeable things not sought for" may bring long-needed "break-throughs" where least expected. Meanwhile, long-term investments in the proven investigator, in interdisciplinary team research, and in projects for the improvement of methodology and quantification continue to add slowly to our knowledge.
The scope of the research supported in mental health crosses through many fields of specialization -- psychiatry, psychology, sociology, anthropology and other social sciences, in addition to such biological sciences as neuroanatomy, neurophysiology, biochemistry, neurochemistry and genetics. As the number and variety of research grants in these areas preclude any comprehensive summary of the research, the following remarks will attempt only to highlight some of the research areas.

Basic and Methodological Research

From the early beginning of the research grants program, the National Institute of Mental Health has believed strongly in the support of basic research -- defined once as "research where the primary aim of the investigator is a fuller understanding of the subject under study rather than a practical application thereof." This year a very substantial share of the research grants program was invested in the support of basic research studies.

During 1957 grant support was awarded for a number of research studies dealing with the functioning and structure of the brain. Through the use of implanted electrodes in an animal brain, one investigator hopes to locate neural systems concerned with basic drives -- hunger, thirst, sex, etc. -- a research study of great potential significance to a neurophysiological understanding of behavior. Another research project approved this year seeks to provide new data on behavior as related to chronic stimulation of cerebral structures. The investigator, who carries out much of his experimentation with a monkey colony at Yale University, utilizes an ingenious, transistor-like brain stimulator the size of a cigarette pack.

Explorations of brain chemistry in animals provide further clues to the sources of behavior. N.I.M.H. research-supported investigators at the University of California are examining brain enzymes in relation to the adaptive problem-solving ability of the animal. It has already been demonstrated that more adaptable animals, those capable of variability in attempting to solve a problem, have a higher level of activity in one of their brain enzymes -- cholinesterase -- than do those less adaptive animals, more rigid in their behavior when faced with a problem. Another grantee, formerly a U.S. Public Health Service fellow, employs both chemical and electrical stimulation of the local brain areas in rats together with electroencephalograph recordings, in a further effort to understand the action of neural centers concerned with primary-drive behavior (sexual, maternal, etc.).

One of our more important needs in psychosomatic medicine is
a widened understanding of the relation of behavior and physiological processes, such as blood pressure, heart rate, muscle potential and other processes controlled by the autonomic nervous system. Modern, polygraphic equipment offers many new tools for measuring and recording performance in the autonomic nervous system, termed by some "the voice of the unconscious." The Institute, for several years, has supported a series of electrophysiological studies of the autonomic nervous system as a mechanism underlying hyperkinetic behavior.

It has long been of theoretical interest whether some persons show the effect of stress mainly through the increased activity of one physiological system, as, for example the cardiovascular, while others reveal the effect of stress primarily in a different functional system, such as the gastro-intestinal or skeletal-motor. A research grant, awarded by the Institute this year, provides for further systematic study of the specificity of physiological reactions to stress. Still another research project utilizes electrical stimulation of the skin in psychophysical studies on man and in parallel electrophysiological work on the cat brain, studying space-time interactions in the somesthetic system.

As yet we have only begun to understand relationships between man's early learning experience and his later behavior. An N.I.M.H. grant-supported study with birds and animals on "imprinting --" an extremely rapid form of learning, which takes place during the early life of many organisms -- is helping to verify and extend some of the original findings on imprinting. Other research projects with monkeys and other animals attempt to clarify the role of fearful experiences with other individuals upon subsequent social behavior, and also investigate the permanency of physiological and psychological effects produced by handling (or gentling) in infancy.

In a world made only too conscious of radioactivity, timely research on the behavioral effects of x-irradiation on animals before birth is being currently supported at the University of Tennessee and the University of South Dakota.

As tools for testing and measurement are improved and other methodological advances made, new roadways of knowledge may open to the research investigator. One substantial "program grant" at the University of Washington supports long-term research in the mathematical analysis of patterns of personal data - investigating such problems as methods for research on diagnoses, factor analysis, and ways of improving psychological tests. This year several additional grants were made in the area of psychometric theory -- including one grant for the preparation of a handbook of contemporary measurement theory.

A substantial amount of basic research in psychopharmacology
has received grant support this year -- in part as the result of direct program stimulation by the Psychopharmacology Service Center, and is elaborated on elsewhere in this report.

Research in Social Problem Areas

Increasingly, in the last decade American society has come to recognize the mental health implications of a number of "social problem areas" -- among them juvenile delinquency, aging, drug addiction, alcoholism, and mental retardation. Together with the developing sense of public responsibility for better solutions to these problems which affect so many of society's members, there has grown an increasing demand on state and national agencies to assist in supporting research in these areas. Last year's Annual Report documented the Congressional interest in fostering research in these social problem areas and pointed in detail to the growth of such research supported by N.I.M.H.

During 1957 the Institute has continued to encourage the submission of well-designed projects, both in basic and applied research relating to the special areas of social concern. Among the more sizeable awards made this year is a grant given jointly with the National Heart Institute to establish an Aging Research Center at Duke University. The Duke program has been especially designed to promote an interdisciplinary research approach to the multiform problems involved in the process of aging.

A variety of other research projects in aging, juvenile delinquency, drug addiction and other problem areas reflect an increasing interest on the part of research investigators throughout the country to work in areas of direct social concern. Considerable progress in stimulating research in psychopharmacology has, of course, been fostered in the Psychopharmacology Service Center, as is reported subsequently.

Other Areas of Research

While the number of grant applications has increased during the last three years at a near geometric rate, much of the overall pattern of grant support has remained relatively stable. An exception, of course, has been the publicly spotlighted area of the tranquilizing drugs. But side by side with the growing interest in special social problem areas, there moves a steady volume of applications for research into such psychological processes and functions as intelligence, learning, perception, attitudes, emotional states and their interrelations, as well as a large body of research directly dealing with the etiology and treatment of mental illness.
Studies of the causes of severe mental disorders, such as schizophrenia, are exploring both genetic and environmental factors. Biochemical approaches, such as research on the metabolism of indole derivatives in schizophrenics, attempt further to establish the etiology of the disease.

Treatment studies continue to range throughout group psychotherapy, psychoanalysis, shock therapy, drug therapy, "milieu" or social setting therapy and a variety of rehabilitation programs. In the face of the recognized nationwide shortage of hospital attendants for the mentally ill, the Institute this year awarded a grant to the American Psychiatric Association to support a working conference on volunteer services for psychiatric patients.

History offers long documentation to the thesis that man acts according to his perception of his environment. Among research studies to enlarge our understanding of the basic features of perception, is a "program grant" to Clark University. Other studies are exploring the judgemental processes involved in perceiving other people.

Both in 1956 and again in 1957 the National Advisory Mental Health Council, conscious of what one leading American medical historian has referred to as a mistaken modern tendency "to limit the definition of research to the experimental process," recommended further support of scholarly research. The Council has also encouraged grant support of research projects in the history and socio-cultural aspects of psychiatry and, more broadly, of medicine.

Several current mental health research projects may also contribute to the great American talent hunt today, through supporting projects for a more systematic analysis of aptitudes. During 1957 the Institute participated in an inter-agency grant award to set up a new study on identifying, developing and utilizing human talents, to be based on a sample of over one million American high school students.

III. THE PSYCHOPHARMACOLOGY RESEARCH PROGRAM

The revival of psychopharmacology, an old science with a new name and with renewed promise of help for the thousands of mentally ill patients throughout the country, led to the establishment in late 1956 of the Psychopharmacology Service Center. During its first year the Center has had to struggle with, and learn to adjust to, the many administrative problems and growing pains experienced by any young organization. It came into being at a time when the "tranquilizing
drugs" had caught the attention of the whole American public. Medicines for the mind and drugs for the soul were -- and still are -- not only the target of cartoons and quips, but also a source of deep concern to scientists, physicians, and all those responsible for research funds and a subject of serious editorial comment by the press and other thinking laymen. With such an urgent and pervading interest in its work, the staff of the Center was plunged precipitously into almost daily crises calling for immediate action and decision. But meanwhile, in this atmosphere of subdued uproar the staff felt impelled to proceed deliberately and soberly with a program leading to its ultimate goal. This goal can perhaps best be stated as the promotion, stimulation, and support of research and related activities that will result in increased understanding of the psychopharmacological agents and their role in the treatment of psychiatric patients. And clearly, from this greater understanding may come the possibility of freeing those with mental illness, whether serious, debilitating and continuous or slight, bothersome, and transient, to live more creative, interesting, and happier lives.

Psychopharmacology Service Center Staff
Activities and Program Developments

At its inception the Center was staffed with two professional persons; at the end of the year there are five professional persons, plus supporting semi-professional, secretarial, and clerical personnel, amounting to a total of thirteen. Staff has not been easy to come by, and much time of those who first came to the Center has been spent in recruiting and other personnel chores.

Soon after its formation, a Psychopharmacology Advisory Committee was selected and appointed. This committee, made up of leading scientists in psychiatry, psychology, sociology, neurophysiology, and pharmacology is responsible for guiding the staff on general policy and planning. It also serves as a review committee for grant applications in psychopharmacology. The staff and the committee have been working through a period of definition of functions, especially in the matter of review functions. After trying several different procedures, it has now been decided that most of the applications for grants in psychopharmacology will be reviewed by this committee, with related basic studies reviewed by the relevant Study Sections.

Conference and Meetings

As part of its effort to facilitate and stimulate sound research, the Center held two conferences in 1957. On January 14 and 15, in collaboration with the American Psychiatric Association, it called together a group of prominent clinical investigators and editors of
scientific journals to discuss problems in the reporting of psychiatric drug studies. The major purpose was to consider ways in which the reports of clinical drug evaluations could be made more informative and useful. The conference resulted in a series of concrete and specific recommendations on reporting of data about patient selection, evaluation of change, treatment setting, and toxicity reactions. In addition, the editors recommended that as one means of handling the flood of psychopharmacological papers a newsletter-type of journal be published, containing brief summaries of current research, analytic review articles, and bibliographies. An article describing the conference entitled "Recommendations for Reporting Studies of Psychiatric Drugs" appeared in the July 1957 issue of Public Health Reports.

Later in the year, on September 19 and 20, the Center organized a working group on anti-depressive or "energizing" drugs. Because the tranquilizing drugs appear to be of only limited value for patients who are depressed, withdrawn, or markedly inactive, several new drugs with potential anti-depressive or stimulant properties are being tried. The staff of the Center deemed it wise to meet at a time when research on these drugs was just beginning, with a group of investigators who have done, or might be interested in doing, such research to exchange views and information and to lay plans for future research. One result of the meeting was the conclusion that problems of research with cases of regressed and withdrawn schizophrenia are quite different from research on depression. Even though the same drugs may turn out to be effective for both groups, the patient populations are, in fact, not at all alike and demand research planning designed for the specific group under study. The animated discussion and large amount of new information gleaned by the Center's staff and all those present demonstrated the value of such working groups as one fruitful approach to stimulating good research.

Informational Activities

As another approach to research facilitation and stimulation and as stated in the Research Grants and Fellowships Branch Annual Report for the Calendar Year 1956, one of the functions of the Psychopharmacology Service Center is to "serve as a clearinghouse of information." During the past year the Center has collected, organized, and catalogued about 2,500 articles and reports, both published and unpublished, on psychopharmacology. A coding system has been developed to permit easy and accurate identification and retrieval of the documents, and most of them have been coded. For over 500 of the more important articles, 300-word abstracts have been written so as to provide investigators with concise, well-organized, and readable summaries of research in
which they are interested. It was originally planned to follow the recommendation of the editors attending the conference on reporting of psychiatric drug studies by starting a newsletter or abstract journal to serve as one vehicle for the rapid communication of information about research activities in psychopharmacology. However, as this notion was explored in more detail, it became evident that administrative considerations militated against the Psychopharmacology Service Center itself handling the publication. The present proposal is to solve this aspect of the communication problem by grant support. Now that investigators know of the existence of the information clearinghouse, many requests for information have been received and answered. These requests have ranged from specific questions about use of drugs with certain kinds of patients to general inquiries about all research that has been done in broad areas of psychopharmacology. Although much of the scientific information activity of the Center has revolved around the accumulation and dissemination of written research reports and the preparation of reference lists and bibliographies, all members of the staff have engaged in providing information by attending scientific meetings, presenting papers, taking part in discussions of psychopharmacology both at scientific conventions and with visitors in the office, answering many telephone inquiries received every day from scientists and administrators both within and outside the government, appearing on television programs, and being interviewed by newspaper and magazine writers. Finally, in line with the request of the 83rd Congress, a comprehensive status report has been written, describing in detail the developments in psychopharmacology during the past year.

Interactions with Drug Companies

Throughout the year the staff has been meeting and corresponding with representatives from many of the drug companies. At the spring meeting of the Physiological Society a presentation was made to a relatively small group of drug company representatives to describe to them the purposes and activities of the Center. A more extensive report was given in October to the American Drug Manufacturers Association. Relevant here also is the fact that the executive secretary of the American Drug Manufacturers Association is a member of the Psychopharmacology Advisory Committee. Relations with the drug companies have been cordial and mutually satisfactory. The companies have shown a sincere willingness to give information (some of it confidential and handled in a strictly confidential manner by the Center's staff) about their drugs, both new and old, and they have cooperated whole-heartedly with the information clearinghouse. The Center, in turn, has sent much general information about psychopharmacology to persons doing research in the drug companies. It has had
many sessions with drug company representatives to discuss their research problems and to consult with them on techniques and methodology, particularly on problems of screening drugs for behavioral effects and designing of clinical studies. These discussions illustrate one important facet of the Center's work. The drug companies do not need financial support, but they often do want good objective evaluations and advice. Since much of the psychopharmacological research is done under drug company auspices, the Center, through its consulting service, can indirectly but very significantly contribute to the development of better research and, thus, to better understanding of the drugs.

**Research in Psychopharmacology**

The core and raison d'etre of the Psychopharmacology Service Center program is stimulation and support of research. During the fiscal year 1957, 42 new grants in psychopharmacology were awarded, totaling $734,291. These grants range in content from basic pharmacological and physiological studies through research on the effects of drugs on animals and normal human behavior, to clinical studies of drug effectiveness in psychiatric patients. In terms of amount of support they vary from small, pilot one-year studies of about $2,000 to five-year support of a major and extensive research program on the psychopharmacology of schizophrenia totaling more than $500,000.

The National Institute of Mental Health has for several years been supporting substantial work in psychopharmacology through its regular research grants program. This work and emphasis are continuing, with the added impetus of additional funds specifically earmarked by the Congress for both preclinical and clinical research in psychopharmacology. Although continuing to push basic research, the staff of the Center and its Advisory Committee have, during the past year, channeled considerable effort into the stimulation of sound, well-controlled clinical studies, and several new grants have been awarded for such research.

One carefully controlled clinical study in a large state hospital system is testing the effects of four phenothiazine drugs on chronic schizophrenic patients. Dosage is individualized and is at the high upper limit to yield needed information about dosage and dosage schedules for future use of drugs in hospital settings. The research is designed to answer the question of whether or not patients treated with drugs improve, as compared with untreated patients, in their social adjustment within the hospital and also to obtain conclusive data on the number of patients who improve enough to leave the hospital. A complementary investigation is studying the effects
of five phenothiazine drugs on newly admitted, rather than chronic, patients. Four of the drugs are the same as those being used in the study of chronic patients, thus allowing a good basis for coordinated and comparative results on these two groups.

Another investigation on acutely ill patients is evaluating the effectiveness of both chlorpromazine and reserpine. In addition to increasing knowledge about the comparative value of these two drugs, this study should extend the generality of the findings about tranquilizing drugs and the applicability of their use. These studies will make possible sound conclusions about drug effectiveness and, also important, will provide information on the best designs to use in future research in hospital settings.

Preliminary observations of results with tranquilizing drugs indicate that some patients respond and others do not. What accounts for this difference? In order to discriminate more clearly the differences and thus to predict more accurately the effectiveness of drugs, a study is underway in which patients will be given several perceptual tests before they begin drug therapy and these tests will be correlated with results of the treatment. This study may well also point up clues leading to better understanding of the mechanisms of drug action in the nervous system.

Many clinical studies have indicated, in a general way, that drugs are of great benefit to hospitalized psychiatric patients, but there has been little research on outpatients. With the release of patients from mental hospitals after drug therapy it is essential to know if these patients are able to take their places as active productive members of society. Consequently, research is being supported to evaluate chlorpromazine and promazine for use with chronic schizophrenic patients treated in a clinic, rather than a hospital. The study is assessing the psychological changes accompanying drug therapy and the patient's social adjustment in the community. Moreover, it is not basing its conclusions on observations for only a few months, but is planning to follow the patients' progress for several years.

Closely related to the question of outpatient drug treatment, is the question of how long to continue drug therapy with chronic patients after their overt symptoms have subsided and they have been released from the hospital. Is it necessary to continue the drugs in the same way that diabetic patients must keep on taking insulin and epileptic patients anticonvulsant medication? Should the drugs be gradually reduced, or should they be replaced by placebos? A well-planned study in which neither the psychiatrist, psychologist, and social worker nor the patients know which kind of treatment is being used is attempting to answer these important questions.
With the tremendous increase in the number of new psychopharmacological agents it is vital that they receive careful preliminary clinical screening soon after they become available. One of the studies is being supported specifically to subject new drugs to rigorous testing. Along with the clinical trials, work is being done on animals to observe any toxic effects after long-term administration and also to obtain data on the possible sites and modes of action of new compounds.

It is a truism that the effects of a drug are not produced just by the drug but by the interaction of the drug with the system in which it is used. This is even more true of psychopharmacological agents, where the interactions extend into complex personality and social variables. One study currently receiving support is comparing drug effectiveness with patients who are merely given custodial care with patients who are receiving intensive social therapy from psychiatrists, nurses, and other personnel. An interesting by-product of this study will test the hypothesis that intensive social therapy may be just as effective as drug therapy.

Not only are the social variables in drug action in need of study, but it is essential to investigate the psychodynamic and personality changes that appear with drug therapy. Therefore, a study has begun in which the patients receiving drugs are also being given intensive psychotherapeutic interviews or are undergoing psychoanalysis.

In such a broad field as psychopharmacology, how shall the many important variables be determined? One investigator is attempting to delineate these variables by analyzing the relations between environmental variables and the effects of drugs. Both animal and human subjects are being used, and a wide variety of measures and techniques employed. As specific reproducible results are found in animals, crucial experiments will be adapted for human beings to learn the generality of the results.

Several researches on drug toxicity are under way. One is working on psychomotor dysfunctions, such as parkinsonism, that occur with use of tranquilizing drugs. Another is looking into the effects of chlorpromazine and reserpine on the reticuloendothelial system to pin down the clinical observation that patients on protracted drug treatment seem more susceptible to infections and are less predictable in their response to antibiotic therapy. Indirectly related to studies of toxicity, but with definite implications, is a study of the effects of drugs on the psychological development of young animals. The significance of this research for the question of using drugs with children is obvious.

In addition to stimulating research and providing support for
clinical and toxicological studies, the Center has during the year encouraged many studies of basic research on animals and of the effects of drugs on the performance of normal human beings.

Plans for the Coming Year

In the process of reviewing applications for research grants, making surveys of past and current research, and consulting on research designs, the staff and its Advisory Committee have become increasingly aware that there are no good instruments for assessing the psychological and social changes that take place with drug therapy. This is particularly true in studies of drug effectiveness with neurotic patients or psychiatric patients who are not hospitalized. Two recently awarded research grants will be concerned with this problem as it involves hospitalized patients. In addition, to meet this need the staff, together with a subcommittee, is devoting considerable effort to the construction of a valid, reliable rating scale for use primarily in outpatients. This undertaking exemplifies one of the practical and significant ways in which staff activity can augment research being done under grant support.

Although there is no lack of preclinical research in psychopharmacology, there is a need for compilation and organization of the data and theories to learn where psychopharmacology has been and where it is going. A recently-begun staff project will be the preparation of extensive and definitive working papers to serve as a basis for program planning and stimulation of research. One of the papers will emphasize the pharmacological and physiological research; the other will be primarily focused on behavioral techniques with animals.

The informational activities of the Center will undoubtedly have to be expanded and extended if the demands of investigators are to be met, and explorations into ways in which the publication problem can be solved will be continued. Hopefully, the foreign literature will also be included in the collection and will be translated and abstracted.

The success of the first two conferences has led to plans for additional meetings. Now under consideration is one meeting to discuss problems of chronic drug administration, including toxic and withdrawal effects. The other will probably be organized around the topic of behavioral testing of drugs.

Finally, now that at least some of its staff and administrative problems appear to be resolved, the Psychopharmacology Service Center can concentrate more fully on its primary function of research stimulation, planning, and accomplishment.
Specific plans are being considered for the organization of single or cooperative studies in the following areas:

1. The testing of new drugs in chronic schizophrenic populations.
2. The evaluation of newer "energizing" drugs in depression.
3. Drug studies in neurotic outpatients.
4. Drug effectiveness in both schizophrenic children and children with serious behavior disorders.

It is probable that work will be under way in most of these areas before the end of the current (1958) fiscal year.

IV. RESEARCH TRAINING: CAREER INVESTIGATOR GRANTS AND THE FELLOWSHIPS PROGRAM

Present day shortages of scientific personnel and the spreading range of professional disciplines involved in mental health research have accentuated the need for training assistance. Research training activities of the Branch as represented by both the Career Investigator grants and the research fellowships program constitute a vital share of Branch activity. This year, with the addition of a full-time Branch staff member for fellowships and Career Investigator grants, a greater degree of planning and program evaluation has been made possible in these programs.

The Career Investigator Grant Program. Started in 1954 as a new form of research support designed to assist in the opening of research careers to qualified young psychiatrists and scientists in related disciplines, the Career Investigator program has supported seventeen investigators to date. All but three are psychiatrists. The program, which aims to enable a limited number of highly qualified young men or women to spend from three to five years in full-time research and further development of research skills, manifests considerable stability by this time.

It is significant, that in the shifting psychiatric world -- where financial rewards for private practice far outweigh any fellowship or training stipend, there have been no resignations from amongst the psychiatrist Career Investigators.

In December, 1957 past and present Career Investigators together with members of the Selection Committee gathered together in a three-day meeting at Arden House in Harriman, New York for a general discussion of the program. The role of the research psychiatrist
is a relatively new one in many university settings, and a share of the discussion was concerned with the professional future of the research psychiatrist. Stressed by many of those participating in the program was the value to the Career Investigator of a strongly organized university department able to offer research guidance. The discussions also emphasized the validity of the three to five-year research training program in terms of the growth of an investigator's research abilities. As a whole, the meeting provided a valuable opportunity for the interchange of scientific ideas among this select cadre of research investigators.

The Research Fellowships Program. During fiscal year, 1957, $647,000 was earmarked for mental health research fellowships. The Mental Health Fellowships Board reviewed 206 applications and made 147 awards. Applications in this lively program range over a wide variety of the behavioral and biological disciplines related directly and indirectly to mental health.

Fellowships supported by N.I.M.H. are available to the scientist whose experience has matured him to train for leadership in mental health research, to the post-doctoral candidate preparing for a research career, to the pre-doctoral student whose endowment recommends him for emphasis on research training, and finally (an innovation of fiscal 1957) to the medical student whose aptitude justifies a year or two of application to the techniques of the basic sciences as an extension of his training for medical work. More than two million dollars has been invested in over 600 mental health research fellowships during the period from 1947 through 1957.

Research work in progress by N.I.M.H. fellows extends to a variety of areas, including the problems of aging, mental retardation, psychopharmacology, neurophysiology and techniques of clinical psychiatry. This year's applications also numbered several studies submitted by educators which deal with adjustment problems in high school and college students.

While the fellowships program has repeatedly proven its value as a sound investment in research training, the administration of the program has been somewhat hampered by the overall volume of fellowship applications received at N.I.M.H. It has been difficult in the past to provide that individualized attention to fellowship applicants which might pay dividends in more responsible and selective faculty guidance. With the addition this year of a full-time Branch staff member to work with the fellowships and Career Investigator programs, it is hoped this recognized problem may reach better solution.
Estimated Obligations for FY 1958

Total: $328,353

Direct: $199,307

Reimbursements: $129,046
During the past year one of the serious problems confronting the overall field of mental health is that of manpower. Because of the expanding interest of the country as a whole in the field of mental health opportunities for staff appointments are increasing at a rate far greater than the capacity of the training centers to prepare professional people. The staff of the Training Branch have been deeply involved in this problem. In addition, attention has been focused upon improving and extending the quality of psychiatric education. Continued emphasis and support have also been directed toward training large numbers of clinical personnel for the reason that it is from this group that we get our people for leadership positions in teaching, research, public service and administration, and for community mental health programs at State and local levels. This does not imply that the Training Branch has neglected giving stimulus to the development of more adequate training opportunities in the area of research. The staff are expending considerable effort in this latter direction and it is anticipated in the next several years more attention and conceivably more grant support will be expended in the direction of developing basic sciences programs in human behavior. A number of medical schools are engaged in a study of the development of a basic sciences department of human behavior at this time.

Aside from the needs for personnel for clinical therapeutic activities is the need for stimulating the development of community mental health personnel for administrative leadership at the State and local community level. These administrative leaders are in extremely short supply and considerable stimulus must be given to the training centers to have them focus their
attention upon the preparation of such professional persons. In the field of mental health the educational centers are experimenting with various types of training programs that will prepare a mental health leader analogous to the general public health officer to deal with the problems of prevention of mental illness and the promotion of mental health.

In connection with these activities, the staff of the Training Branch carry on extensive consultation with presidents and deans of universities, medical schools, graduate schools and schools of public health as well as with department heads in psychiatry, psychology, social work and nursing. Frequently the staff have been called in consultation or have been used as resource personnel in the broad field of mental health education. The number of project site visits approximated 300 made by the staff during the past year.

Grants have been made during the past year for the purpose of improving and extending the psychiatric aspects of training of the medical and nursing student. These people represent a first line of defense so to speak and it is desirous from a preventive point of view that they be adequately prepared to deal with emotional problems encountered in their respective spheres of activity.

During the past year traineeships were awarded departments of psychiatry in medical schools for the purpose of providing additional clinical experience in psychiatry or experience in psychiatric research for the medical student. It is anticipated that more physicians will be recruited into the specialized area of psychiatry. A total of 290 such traineeships were awarded.

As indicated above there continues an excessive demand for leadership people in teaching, research, public service and administration, and
in community mental health activities. These people come from the programs of clinical training. For this reason the greatest percentage of the funds available for training have gone into the preparation of as large numbers of psychiatrists, psychologists, social workers, and nurses as is possible. During the past year frequent consultation has been given to a number of schools of education concerned with the preparation of the classroom teacher. These schools have been interested in incorporating material from the field of the behavioral sciences, including psychiatry, psychology, and social sciences into the training of the classroom teacher that will be useful to her in dealing with emotional problems encountered in the growing and developing child in the classroom setting. It is anticipated that several of these institutions will apply to the Institute in the near future for support of programs of an experimental nature to work out the content and the methods for presenting this material in these training programs. Special attention continues to be devoted to encouraging the development of training programs concerned with mental retardation and juvenile delinquency. Some small encouraging progress can be reported in these latter areas.

A large number of training centers, widely scattered throughout the country, appear to have increasing interest in these conditions. We cannot report the same kind of interest in the training of personnel to work in the area of alcoholism. It has been a difficult assignment to arouse interest in training personnel for this health problem.

In a number of medical schools there appeared during the past year a considerable interest in developing a closer teaching liaison between the departments of psychiatry and the pre-clinical or basic sciences departments.
This interest seems more intense from the pre-clinical departments of pharmacology and physiology. A number of medical schools are experimenting with conjoint teaching activities involving the department of psychiatry and one or more of the pre-clinical departments. It is anticipated that the Institute will receive in the future requests to support the further elaboration of these conjoint experimental teaching activities.
Training and Standards Branch

BUDGET SHEET

Estimated Obligations for FY 1958

Total: $410,081
  Direct: $278,823
  Reimbursements: $131,258

Project included: Training Activities
Estimated Obligations for FY 1958

Total: $221,945

Direct: $170,533

Reimbursements: $51,412

Projects included: M-D(C) 1 through M-D(C) 3
Project Title: The Analysis of the Psychotherapeutic Process, Particularly the Psychoanalytic Process

Principal Investigator: Robert A. Cohen

Other Investigators: David Shakow, Allen Dittman, Morris Parloff, Paul Bergman, Mabel Cohen

Cooperating Units: Laboratory of Psychology

Man Years:

Professional: 0.25

Project Description:

Objective: To conduct an intensive study of the psychoanalytic process

Methods Employed:

1. Data Collection: Naturalistic recording by motion pictures and stereophonic sound of portions and of complete courses of psychoanalytic (and in some cases of other psychotherapeutic) treatments of adults and children with a variety of emotional disorders.

2. Data Analysis: Methods will be developed to organize the extensive material which will be gathered by a variety of partial, total and cumulative exposure techniques; to divide it into units which on the one hand accurately reflect the nature of the exceedingly complex interactions between patient and therapist, and on the other are sufficiently specific and manipulatable to permit an orderly and meaningful analysis of the therapeutic process.

For the past 2 years two training and supervising analysts have studied very intensively a short series of therapeutic interviews: first using a typescript alone, then the sound recording and finally the sound motion picture. These studies were carried out independently at the beginning, but they are now being combined in order to set up categories for the individual elements which must be rated in order to study the therapeutic process.
Project Description (continued):

Patient Material:

Up to the present time the material used has been collected at the University of Illinois where another research group is working toward the same goal. Our own physical set-up has finally been completed, and an experienced therapist has begun a trial series of single interviews with a variety of patients and with several normal controls. In the coming year it is anticipated that it will be possible to embark on a motion picture recording of a regular psychoanalytic therapy.

Major Findings:

None as yet. Much methodological research must be done before substantive theoretical contributions can be made.

Significance:

This is one of a series of studies of the psychotherapeutic process: The Process of Change and the Communication of Value Systems in Psychoanalytic Therapy M-F-P(C) 5; Linguistic Study of Emotional Expression M-P-C(C) 4; Judgment of Facial Expression from Short Sequences of Motion Picture Film M-P-C(C) 5; Analysis of the Psychotherapeutic Process: The Cumulative Information Derived from Repeated Viewing of Complex Material M-P-C(C) 2; Development of an Ego-Integration Conceptual System for Studying Psychotherapy M-F-P(C) 6.

Despite the fact that psychotherapy is the major therapeutic device in psychiatric treatment, our understanding of it as a process is still very limited. One reason for this is that previously data could be secured only by the therapist; his reporting was limited both by the fact that he was a participant as well as an observer in the process and also by the human impossibility of reporting completely what had transpired. In the therapeutic situation, the relationship is exceedingly complex, and this is all the more true since much of the communication occurs at an implicit level. Hence, much of the significant data was not even available to anyone outside the relationship which it was proposed to study. The sound motion picture provides for the first time a sizable and significant amount of objective data hitherto unobtainable; what is equally important is that this data is collected in a form suitable to multiple and repeated analyses.
This series of studies may make many contributions methodologically, it will be possible to study the psychoanalytic process scientifically to a far greater degree than has heretofore been possible. Theoretically it is expected that it will make available new and highly significant data - data which is gathered in a more or less naturalistic setting but which is as objective as those usually obtained in laboratory experiments.
Beyond the direct contribution to a better understanding of the psychotherapy process itself, it will aid in the establishment of
Project Description (continued):

Significance (continued):

the scientific bases of psychoanalytic theory. It is safe to say that psychoanalysis is one of the central socio-psychological sciences. It deals with man, born with his drives and abilities, with his slow adjustment to social life through family training. While it deals with the same kind of data social sciences deal with, it also provides information on the subjective aspects of the activity of those parts of the central nervous system which have recently attracted so much attention, viz. the limbic system and the reticular activating system. Psychoanalysis should be able to make fundamental contributions to the understanding of education in its broadest sense.

Proposed Course of Project:

It is expected that this program will continue for many years.
Part A.

Project Title: Development of an Ego Integration Conceptual System for Studying Psychotherapy

Principal Investigators: D. Wells Goodrich, M.D.
Donald S. Boomer, Ph.D.

Other Investigators: None

Cooperating Units: Section on Personality, Laboratory of Psychology
Laboratory of Clinical Sciences
Employee Health Service, NIH
Community Psychiatric Clinic, Rockville, Md.
Washington Institute of Mental Hygiene

Man Years (calendar year 1957): 2.00
Patient Days (calendar year 1957): 42 patient days
Total: 2.00
Professional: 1.00
Outpatients: 42 patient days
Other: 1.00

PROJECT DESCRIPTION:

Objectives: (1) Long-term: To develop a theoretical model and observational tools for the purpose of generating and testing a network of hypotheses about the conditions of personality change. (2) Immediate: To organize a loose set of clinical-theoretical ideas and observations into a coherent model, as indicated above, and to determine the feasibility of observing certain critical changes in patient behavior during psychotherapeutic sessions.

We are concerned with the moment-to-moment level of ego integration in the patient in his dealings with the therapist. We have conceptualized and hope to be able to identify in action four patterns of ego integration among which patients are presumed to shift during a therapy session. These have been carefully spelled out, but for the purpose of this report brief descriptive summaries must suffice:
Defended (F) - The patient is controlling anxiety by his customary means, and is functioning at his characteristic level, involuntarily revealing from time to time, the ego-
distorting aspects of his defensive functioning. Partially defended (P) - Similar to F but less stable and comfortable. Patient displays some readiness to move toward a suspension of his defenses, with concomitant premonitory anxiety.

Self observing (o) - The widely-described "split ego" state in which the patient is monitoring his own behavior and considering simultaneously, or in rapid alternation, his feelings, his behavior, and his defenses.

Decompensated (C) - The overwhelmed ego: Anxiety is so high as to submerge defenses, disrupt some or all ego functions and interfere with interpersonal and task-directed functioning. This may be a clear open panic state or a transitory disturbance, virtually unnoticeable unless reported by the patient.

Methods Employed: In order to provide data on personality change during psychotherapy, from two to six patients are maintained in outpatient psychotherapy continually. The senior investigator is responsible for maintaining professional relationships with the referring and collaborating agencies (see "cooperating units"), for supervising the diagnostic screening procedures (psychiatric interviews, psychological tests, physical examinations and laboratory tests), and for supervising the psychotherapeutic treatment and incidental medical care provided to the patients while they are subjects. Psychiatric supervision of psychotherapy is carried out by means of individual conferences with the project's therapists (i.e., psychiatrists and psychologists who donate time to the project) and by use of the one-way vision screen when this is indicated to clarify a clinical problem.

During the first few weeks of psychotherapy, and periodically thereafter, each patient's major resistances are formulated both in general clinical terms and in terms of specific interview behavior. Particular attention is directed to formulating major current transference resistances, since the research model focuses upon the process of patients' attaining conscious insight into transference experiences. All interviews are recorded for behavioral analysis, according to the methods outlined in Project No. M-P-P-(C)-6 (Section on Personality, Laboratory of Psychology).
Interview transcripts are also coded into phases according to whether the patient's statements demonstrate a blatant resistance state (F) or one of the other ego states (P, C, or O). It may then be possible to explore relationships between the clinical course of therapy, specific ego state phases during interviews and the profile of statistically measurable behaviors.

Through this integration of clinical case studies with the statistically-controlled behavior measures, we hope to be able to define shifts in the patient's ego state. Subsequently, it may also be possible in a more detailed theoretical manner to relate our concept of ego state to more general concepts of ego psychology.

**Patient Material:** Patients are selected according to the following criteria: (1) Ages 17 to 40; (2) approximately half women and half men; (3) absence of psychotic or "borderline" type of psychopathology; (4) absence of social or family problems or of severe acting-out tendencies; and (5) likelihood of demonstrating in a short time some definite changes under the influence of psychotherapy. A total of seven patients have been studied to date; the addition of from two to four more patients during the coming year is contemplated.

**Significance to NIMH Research:** The systematic investigation of relevant aspects of psychotherapy is a salient part of the program of NIMH. This project may contribute directly to this effort with substantive findings or indirectly with methodological and conceptual developments which can be utilized in other parallel investigations.

**Proposed Course of the Project:** This work, as currently envisaged, will continue throughout this year and well beyond. Some carefully controlled definitive work will be carried out during this year with regard to the incidence of speech disruptions and the correlates of high and low incidence. The broader conceptual-theoretical work of formulating a model will also continue along the lines outlined above.
Part A.

Project Title: Establishment of a Near Zero Level of Physical Stimulation and of Action Possibilities and its Effects on Mind and Brain Activity.

Principal Investigator: John C. Lilly.

Other Investigators: Thelma W. Galkin and Jay T. Shurley.

Cooperating Units: None.

Man Years:  
Total: .99 1/3  
Professional: .49 1/3  
Other: .50

Patient Days: None

Project Description:

Objectives:
1. To make a survey of the literature on individuals who were exposed to environments in which the physical stimuli were at a minimal level.
2. To devise an environment producing minimum possible levels of stimuli in terms of light, sound, gravitational effects, movement, temperature changes, pressures on the skin, etc.
3. To observe the effect of this environment on monkeys and human subjects.
4. To obtain fundamental base line data on brain activity and mind activity during a state of minimal inputs to the brain from the environment.
5. To interest professional psychiatric and psychoanalytic personnel in serving as subjects to obtain professional evaluations of and maximum meaning from this type of experiment.
6. To write a book detailing our findings in the literature on autobiographical accounts as well as experimental results found by others.

Methods Employed:
1. Library research.
2. Communication with persons who have been exposed to minimally stimulating environments, i.e., American Speleological Society, Arctic Institute.
3. Experimental methods have been under development for the last 4 years. The present approach is to suspend the subject in quiet water,* in the dark at such a temperature as to be neither warm or cool (about 34.5°C) with a breathing mask which gives minimal stimulation. The mask has been the major problem: underwater masks from the Navy Experimental Diving Unit, the Army Engineers, and Chemical Warfare have been found to have too high unit pressures on small areas of the face, leading to (1) pressure stimuli and (2) eventual local anoxemic pain. Therefore, a program of mask development has been undertaken: Model #7 is almost completely satisfactory. Preliminary designs for a quiet, pressure-balanced respirator are being done.

Major Findings: To date, many examples have been found in the literature of individuals isolated in boats or in the polar regions or in prison, but the factors of threat to life, cold, hunger, thirst, sun, etc. make it difficult to attribute the effects solely to reduction of the ordinary levels of stimuli.

The results of experiments done on volunteers show the following:

1. Any remaining continuous stimulus becomes extremely irritating and leads the subject to terminate the experiment.
2. Patterns of activity resulting from previous stimuli slowly die out in the tank—the "half-life" seems to be about 1/2 to 1 hour.
3. A powerful tension may develop in an interval as short as 2 hours.
4. One experience of the first stages of visual hallucinatory phenomena has been experienced.
5. At emersion, the subject's appreciation of clock time was changed so that he felt as if the day was started afresh.

An additional subject has been trained and is about to start his own series of observations on himself.

* Tank devised and its use loaned by Physical Biology NIAMD, Dr. Heinz Specht.
Art A. (continued)

Significance to Mental Health Research: An evaluation of the significance of the literature on normal individuals who have been exposed to extreme environments.

This project will provide baseline data on effects of short-term isolation from the usual levels of stimulation. Since the work is essentially exploratory, we will be in a better position to evaluate its significance after satisfactory apparatus allows better experiments.

This work may allow us to more sharply distinguish between the effects on a normal person of purely voluntary isolation from physical stimuli and that of the involuntary isolation experienced by the mentally ill person; no systematic examination of such effects has yet been made; it may be that certain experiences in these circumstances are fundamental and characteristic for both the normal and the mentally ill person--the major differences may be due to attitudinal variables only. If so, the results may add to our basic understanding of causal factors in mental illness.

A truly surprising amount of interest has been aroused in scientific and non-scientific circles over the reports on this project. During this year interest has been expressed in this project by two groups, one is the submarine warfare group with the Navy and the other is the "Far Side" project group of the U. S. Air Force who are interested from the standpoint: (1) isolation of a man in a space ship, (2) the effect of weightlessness upon his mental functions. Several laboratories have expressed enough interest to warrant their starting similar projects: University of Utah, Mayo Clinic, Holloman Air Force Base, Fort Ord (Human Resources Board).

Proposed Course of Project: 1. To foster the development of a new tank more suitable for these experiments.
2. Continue the search of the literature.
3. To collect data from more subjects.
4. To continue to reduce the stimuli.

Art B included Yes _x_ No ___
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:

Lilly, John C  Some thoughts on brain-mind, and on restraint and isolation of mentally healthy subjects. (Comments on "Biological Roots of Psychiatry" by Clemens E. Benda) J. of the Phila. Psychiatric Hospital, 2:16-20, 1957.
Estimated Obligations for FY 1958

Total: $757,410

Direct: $170,065

Reimbursements: $587,345

Projects included: M-AP(C) 1 through M-AP(C) 12
Part A.

Project Title: The Study and Treatment of Schizophrenia as a Family Problem

Principal Investigator: Murray Bowen, M. D.

Other Investigators: Robert Dysinger, M. D., Warren M. Brodey, M. D., Betty Basamania, M.S.W.

Cooperating Units: None

Man Years (calendar year 1957): 4

Patient Days (calendar year 1957): 2,950 days

Total: 4

Professional: 3

Other: 1

Project Description:

The project was started 38 months ago. The first two years there were major changes in the hypothesis and in the treatment approach to schizophrenia. This is the first year there has not been a major change to include in the annual report. To summarize briefly, the first year was devoted to the study of mothers and patients. The second year was devoted to the study of families with fathers, to a redefinition of the hypothesis, and to efforts to develop a psychotherapy of the family as a unit. The third year went to refinement of the psychotherapy and an effort to define some of the concepts and to write about experiences that had been hurriedly passed over in the emotional turmoil of the first two years. When the project was started, there was no previous literature or experience to use as a guide. There was an intellectual conviction that this area could be profitable. The only blueprint, for an operation that would make it possible for normal family members to continue to live in the high anxiety and for staff to work with the project, was a theoretical anticipation of problems along the way and some ideas about possible solutions. Many decisions that affected the entire course were fortuitous ones to deal with the emotional emergency of the moment. Such was the decision to put the entire family together into a family unit psychotherapy. Originally conceived as an emergency measure to control uncontrolled emotion, it opened up a new area of observations, techniques and concepts.
Objective:

The immediate research objective is to attempt to define in more detail some of the many promising clinical findings that were bypassed in the emotional emergency of the early stages. The therapy objective is further development and refinement of family unit psychotherapy. A therapy objective to reach a more predictable and efficient means of therapy is a crucial part of the project.

Method:

Small complete family groups which include at least father, mother and schizophrenic patient are hospitalized. The hospital setting permits around the clock observation of the family group. The daily family-staff group meetings serve as a means of further check and understanding of the emotional processes within the group, of the emotional conflict between staff and families, of the emotional process within the family, and as a means of psychotherapeutic communication to the family. An inpatient operation is much more difficult to operate than an outpatient operation but the added information and observation is considered essential. On the other hand, there is evidence that outpatient psychotherapy can be more productive than in the inpatient operation. Several outpatient studies have been carried out in order to observe variations and refinements in family psychotherapy. It is possible to try such variations as the use of one therapist with one or more families; or two or more therapists with one or more families.

Patient Material:

Four family groups participated in the 1957 operation. The first was a mother and daughter connected with the project since November 1954. They lived together on the ward into May 1957 at which time they were discharged from the project. They now live at the family home in another state. The second was a mother and daughter who lived constantly on the ward from November 1954, until discharged to outpatient status on October 7, 1957. They live in a nearby city. The third was a family of father, mother, patient, and normal sibling admitted in December 1955 and still active in the project. The normal sibling has been away at school most of the year. The family is currently disrupted by the mother's 3 month "business leave" to their home in another state. The fourth is a father, mother, patient, normal sibling family admitted in August 1956. The family group has been present the entire year except for the normal sibling's absence at school for six months. This family may terminate project participation January 1, 1958. An outpatient family of father, mother, and psychotic teen age daughter have been seen as outpatients since early November 1957. The four inpatient families are the same referred to in the 1956 report.
Project Description: (continued)

It is expected that 2 new inpatient families will be admitted by December 1957, that new families will be admitted as vacancies occur in the ward, and that some outpatient families may be started in 1958.

Major Findings:

1. The clinical facts reported in the 1956 annual report, which could be classed as Intrafamily Reaction Patterns are still as prominent and pertinent as a year ago. These are part of many such observations awaiting more careful definition and incorporation into papers. There is a new series of observations to suggest that the psychotic symptom in the patient is an outward expression of a regressed impulse in a parent.

2. A new class of prominent clinical findings might be classed as "Family Group Reaction Patterns". The families all present a group picture of helplessness and inadequacy. They deal with many life problems as burdens to be endured rather than problems to be solved. Therapeutic emphasis is directed at this helplessness. When either parent is able to become active in solving such a problem, the emotional adjustment of the entire family changes. The schizophrenic patients have responded favorably to actions by parents that popular concept would call traumatic. This suggests that it is not traumatic action but passive lack of action that is incapacitating to patients.

Significance to Mental Health Research:

It may be that the broader perception of psychological processes provided when the family is seen as a unit, may be a major contribution from this project. A medical orientation to help the patient places the fact of a parent's activities in regard to the patient in a completely different perspective than when the orientation is toward helping the family unit. When the project staff is able to achieve a family unit orientation, the investigator has the experience of observing what appears to be a new psychological phenomenon. If it is possible to clarify some of the profusion of clinical facts observable from this perspective, this might become the basis for a different view of interpersonal processes.

Proposed Course of Project:

1. Complete the evaluation and organization of data already secured.
2. Continue the inpatient operation with 3 to 4 complete small families using the same theoretical orientation and treatment approach as a year ago.
3. Build up an outpatient service for variation and development of therapy techniques and to complement the inpatient service.
4. Make an effort to define and conceptualize some of the major clinical findings by-passed in the effort to establish the project.
5. Seek help from other disciplines in the further effort to conceptualize and validate findings.

Part B included: Yes
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project: None

Honors and Awards relating to this project:

1. "Study and Treatment of Five Hospitalized Family Groups each with a Psychotic Member". Invitation to present paper about project to Section on Intrafamily Relationships.

2. "Family Participation in Schizophrenia". Murray Bowen, M. D., Invitation to speak to Psychiatric Staff, Phipps Clinic, Johns Hopkins University, Baltimore, March 12, 1957.


6. Invitation to speak at the Zurich Conference - not accepted.

7. "Schizophrenia and the Family", Murray Bowen, M. D., Invitation to present paper about project at Iowa-Nebraska Psychiatric Meeting, University of Iowa, Iowa City, Iowa, October 26, 1957.


9. Group for the Advancement of Psychiatry, Family Committee, Murray Bowen, M. D., April 5, 6, 7, 1957. Invitation to meet with Family Committee. November 7, 8, 9, 10, 1957, Murray Bowen, M. D., Invitation to become permanent member GAP Family Committee.
Part A.

Project Title: Investigation of the Character Structure in the Alcoholic Patient

Principal Investigator: Murray Bowen, M. D.

Other Investigators: None

Cooperating Units: None

Man Years (calendar year 1957): 120 hours

Patient Days (calendar year 1957): None

Project Description:

This is a detailed psychotherapeutic study of addictive character (alcohol and drug addiction) patients. Five patients have been studied in about six years.

Objective:

Treatment of the addictive patient with a modification of psychoanalytic technique and a study of the character structure of the patient as revealed in the transference relationship.

Method:

Psychotherapeutic treatment using a specific modification of technique based on psychoanalytic theory. The addictive personality is seen as one of the clearest examples of fixation at the oral passive stage of psychosexual development. According to the theory, the relationships of a child at this age centers about the child in the oral receiving role and the parent in the oral giving role. In experience it is very difficult to get a workable transference relationship with addictive patients. The modification in technique involves an oral giving attitude on the part of the therapist and the symbolic oral giving of the therapeutic hour to the point of establishment of a workable transference which is then resolved in the usual way.

Patient Material:

One patient is currently in the study. She was discharged to outpatient status in July 1957.
Project Description (continued):

Major Findings:

Treatment goes satisfactorily both in terms of treatment response and in terms of content material. Indications are that much of the perverse sexuality content is a defense against oral passivity.

Significance to Mental Health Research:

It is hoped that this study may eventually make some contribution to understanding the relationship of oral passivity to other very infantile clinical problems.

Proposed Course of Project:

Continue with this one patient and make a report at the termination of her treatment. It is proposed to keep the side interest in this problem for its contribution in the understanding of the oral passive component in schizophrenia and other infantile character problems.

Part B Included: No
Part A.

Project Title: A Study of Clinical and Experimental Depersonalization:
The Effects of Psychotomimetic Drugs on Psychological Processes

Principal Investigator: Charles Savage, M.D.

Other Investigators: Juliana Day, M.D.

Cooperating Units: Margaret Toohey, Research Assistant; Nursing Personnel
on Ward 3-West

Man Years (calendar year 1957): Patient Days (calendar year 1957):

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Project Description:

Objectives:

To study artificially induced psychoses and delineate their
relation to schizophrenic processes and depersonalization, and
their effect on the therapeutic process.

Methods Employed:

Psychotomimetic agents such as LSD, mescaline, are given to
patients in psychotherapy and to volunteer subjects. Their verbal
productions before, during, and after are recorded, compared and
analyzed.

Major Findings:

A. 1957--Preliminary trial with one psychotomimetic agent
produced an effect more similar to a natural psychosis by creating
a disturbance of thought processes with relatively little visual
disturbance in contrast to the effects of LSD and mescaline.

B. Data collected from 1955 to 1957 on a single patient in
intensive individual therapy who received LSD and reserpine and
Major Findings (continued):

other drugs over a long period of time analyzed for their effects on psychotherapy. Findings: Under the influence of LSD the memories of childhood experiences and emotions which came to the fore were frequently too highly charged to be effectively dealt with in psychotherapy.

Significance to Mental Health:

A. Drugs which are psychotomimetic are useful adjuncts to the study of natural psychoses.

B. The value of LSD in psychotherapy still remains debatable.

Proposed Course of Project:

Further review of data from study "B" with a view to publication. Paper to be concerned with the psychodynamic effects of both LSD and reserpine in the long-term intensive psychotherapy of a single patient.
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:

Honors and Awards relating to this project:

"Lysergic Acid Diethylamide and Schizophrenia," by Charles Savage, M.D. Presented by Dr. Savage at the Association of Former Internes and Residents of Freedmens Hospital, June 6, 1957.
Project Title: A Study of Tranquilizing Drugs: The Effects of a Tranquilizing Drug on Psychodynamic and Social Process

Principal Investigator: Charles Savage, M.D.

Other Investigators: Julianna Day, M.D., Lyman G. Wynne, M.D., Leslie Schaffer, M.D., and Harold A. Greer, M.D.

Cooperating Units: Margaret L. Toohey, Research Assistant; Nursing Personnel on Ward 3-West

Man Years (calendar year 1957): 1.5
Professional: .8
Other: .7

Patient Days (calendar year 1957): 1725

Project Description:

Objectives:
An intensive study to assess the effect of tranquilizing drugs on the therapeutic process.

Methods Employed:

A. 1955-56. Four regressed patients who had been studied and treated intensively for a year's time without tranquilizing drugs were selected. They had all proven resistant to psychotherapy and intensive nursing care. Their daily living, their relations with others and the reaction to the therapist all had had careful scrutiny. Gross behavioral observations were recorded as well as ratings. Comparison of therapy with and without reserpine were made. Double blind controls were used.

B. 1956-57. A fifth patient was added to this study who, in contrast, was a borderline neurotic, who was highly verbal and active in psychotherapy. This patient's therapy had been under observation for over a year with a single therapist, in part with LSD (see project on psychotomimetic drugs). Two periods of reserpine administration with differing dosage were alternated with periods of placebos and
Methods Employed (continued):

phenobarbital administration. Control periods without reserpine were increased over the earlier study from two weeks to a month as previous findings indicated a long lag in reserpine effect.

C. 1957. Two of the patients in study "A" were given clinical trials with chlorpromazine and with Trilafon.

Major Findings:

Further study of data from "A": With reserpine, patients were more friendly and less preoccupied and showed greater self-control and social conformity. Delusional material was less frequently expressed in waking life and appeared in dreams. Individual psychotherapy was a more agreeable collaboration but sensitive topics were still avoided. Reserpine had a dramatic effect in a therapeutic milieu affecting favorably not only the patient but the patient-staff interactions. It did not facilitate psychotherapy within this sample of patients. Its effect did not last after reserpine was discontinued and could also be reversed by severe environmental stress.

Findings from study "B": Analysis of behavior charts and psychotherapeutic interviews showed no significant beneficial shift during reserpine periods. In this patient there was an increased preoccupation with the need for mothering and support during the period of reserpine administration. The patient's periods of greatest curiosity and responsibility were when no drug was administered.

From study "C": The clinical trial with chlorpromazine was for too short a period to draw conclusions and was replaced by Trilafon because of chlorpromazine's undesirable side effects. Neither patient showed striking changes with Trilafon, one showed little or no behavioral change, the other, who had had Parkinsonism with reserpine had no such effect with Trilafon. On maximum doses of Trilafon she was less anxious and more self-controlled than when on no drug.

Significance to Mental Health:

Both studies "A" and "B" are limited by number of patients and by diagnostic category and conclusions must be viewed with caution. In the first study reserpine aids in increasing the psychotic's self-control and social conformity and in both studies reserpine appears to strengthen the patient's repression of conflict, but apparently not facilitate psychotherapy.
Proposed Course of Project:

Further review of data from study "B" with a view to publication. Paper to be concerned with the psychodynamic effects of both LSD and reserpine in the long-term intensive psychotherapy of a single patient.

Part B included  

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Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:

Savage, C. and Day, J., "The Effects of Reserpine on Psychodynamic and Social Processes." Presented by Dr. Savage in May 1957 at the Annual Meeting of the APA. Accepted for publication in the A.M.A. Archives of Neurology and Psychiatry.

Honors and awards relating to this project:
PHS-NIH
Individual Project Report
Calendar Year 1957

Part A.

Project Title: Problems of Psychoanalytic Research with Schizophrenics

Principal Investigator: Charles Savage, M.D.

Other Investigators: Juliana Day, M.D., Harold A. Greenberg, M.D., Leslie Schaffer, M.D., Jordan Scher, M.D., Lyman C. Wynne, M.D., Stewart Perry

Cooperating Units: Nursing Personnel of 3-West

Man Years (calendar year 1957): Patient Days (calendar year 1957):

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Project Description:

Objectives:

1. To study alterations in psychoanalytic technique which are imposed by the research setting.

2. To study the application of psychoanalytic techniques to the therapy of schizophrenics.

3. To study the emotional problems of the therapist brought about by the intensity of the psychotherapeutic relationship with the schizophrenic.

Methods Employed:

Tape recordings of psychoanalytic therapy, staff review and discussions of recordings.

Patient Material:

Hospitalized schizophrenics.

Major Findings:

The transference psychosis which develops in the course of the analysis of hospitalized schizophrenics tends to become diffuse and...
Major Findings (continued):

projected to other members of the staff, and thus converted into a formidable resistance. If the staff responds to the transference distortions as realities, the patient loses the opportunity to learn the nature of the distortion and to develop more appropriate patterns of reactivity. Close cooperation of the analyst with the rest of the staff is essential to the handling of the diffusion of transference.

Customary focus in psychotherapy is on the problems of the schizophrenic patient. Yet equal attention should be paid to the problems of the analyst who is treating him. The analyst's understanding of his own countertransference to his schizophrenic patient leads to an understanding of the patient's productions in analysis and the ability to respond to them appropriately. By identifying with the patient, the analyst is able to understand and communicate with the patient. This process of identification is fraught with anxiety because the analyst experiences the patient's problems as his own and the anxiety associated with them. In addition, the very fact of conducting analysis in a research hospital complicates the transference picture and renders difficult the adherence to a rigid psychoanalytic technique.

Significance to Mental Health:

Psychoanalytically oriented therapy is regarded as a major research tool for the understanding of the schizophrenic process. That which enhances our capacity to use these techniques effectively has both research and therapeutic application.

Proposed Course of Project:

Because Dr. Savage has departed for a year's leave of absence, his focal interest in this area of inquiry will be missing, but attention to these problems will continue as part of several projects, especially the studies of the family relations of schizophrenics.
Part B: Honors, Awards and Publications

Publications other than abstracts from this project:

Savage, C., "The Diffusion of the Transference-Psychosis in the Treatment of Schizophrenia." Accepted for publication in Psychiatry, 1957.

Honors and Awards relating to this project:


Savage, C., "Methodology." Presented at the Annual Meeting St. Elizabeths Hospital, May 4, 1957.


Part A.

Project Title: Family Relations in Schizophrenia

Principal Investigator: Lyman C. Wynne, M.D., Juliana Day, M.D., Leslie Schaffer, M.D., and Stanley Hirsch, M.S.W.

Other Investigators: Harold Greenberg, M.D., Nursing Personnel on Ward 3 West, Morris B. Parloff, Ph.D., Joseph H. Handlon, Ph.D., Donald S. Boomer, Ph.D., Marvin Waldman, Ph.D., Morris Rosenberg, Ph.D., Leonard I. Pearlman, Ph.D.; I. M. Ryckoff, M.D., Consultant.

Cooperating Units: The methods and conceptualization of this project are different from those of any other PHS project. The general subject matter, family relationships of schizophrenics, is similar to project M-AP(C)-1, which, however, solely uses group methods to study the families that generally live on the ward. The present project differs by its use of data from individual family members as well as observation of interaction among the family members. As each project develops further, it is probable that the clinical material and hypotheses from each will complement one another so that comparative discussion should be increasingly fruitful.

One of the families being studied in this project is also involved in project M-SD-5; in the present study, this family has been considered intensively from the standpoint of the dynamics of the family organization as a whole, particularly in relation to the general hypotheses of this project.

Man Years (calendar year 1957): 3.0

Patient Days (calendar year 1957): 1460

Professional: 2.25

Other: .75

Project Description:

Objectives: This project is part of a long-range program of which the central goal is to examine the part that the family setting has in the genesis, form, and course of schizophrenic illness. This research has progressed from intensive pilot studies of a small number of families of schizophrenics to the formulation...
Objectives (continued):

of a series of preliminary hypotheses, which, in turn, have stimulated current planning of further empirical research that will include a critical evaluation, modification, and expansion of these hypotheses.

Methods Employed:

(1) Data collection. Data was collected by tape-recorded psychiatric interviews with the patient, parents and other significant relatives and friends. This included intensive psychotherapy with the patient, and interviews with parents which centered on their participation in the therapy of the patient and which sometimes eventuated in psychotherapy. Collated data was collected from ward administrator and nursing personnel regarding interaction of the patient with ward personnel and of the parents with the ward staff and with the patient.

(2) Analysis of Data. Chief methods of analyzing the data used thus far include the use of the psychoanalytic viewpoint to examine the dynamics of the individual relationships, and modified role theory as basis for analyzing the family system of interrelationships.

Patient Material:

Patient material has consisted thus far of young recently ill schizophrenics with both parents available for outpatient interviews. Five families have been studied thus far.

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<tr>
<td>Number of Patients (Hospitalized)</td>
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<td>Number of parents (Out-Patients)</td>
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Major Findings:

The starting point in the series of hypotheses now formulated was an examination of the quality of interpersonal relations in the families of certain schizophrenics. According to this conceptualization, the acknowledged relations in these families in the pre-psychotic phase have a quality of intense and enduring pseudo-mutuality. Pseudo-mutuality involves a sense of relation which hinges upon fitting in with what are assumed to be the expectations of others; inversely, the sense of relation is experienced as possible only by excluding recognition of any divergence from this fitting together, or complementarity, of reciprocal expectations.
Major Findings (continued):

Pseudo-mutual complementarity is contrasted with mutual and non-mutual forms of complementarity. This differentiation involves a new extension of role theory which was a by-product of this work.

In the families of certain schizophrenics, it is hypothesized pseudo-mutuality takes an especially intense and enduring form in which the family members strive for a sense of relation by trying to fit into the family role structure. The social organization in these families is shaped by a pervasive familial subculture of myths, legends, and ideology which stress the dire consequences of openly recognized divergence from a relatively limited number of fixed, engulfing family roles.

The shared, familial efforts to exclude from open recognition any evidences of non-complementarity within the pseudo-mutual relation become group mechanisms that help perpetuate the pseudo-mutuality. In the families of schizophrenics these mechanisms act at a primitive level in preventing the articulation and selection of any meanings that might enable the individual family member to differentiate himself from the family role structure.

It is hypothesized that the resultant patterns of interpersonal perception and communication, after having become a part of the offspring's personality structure, involve a kind of fragmentation and confusion of experience and thought which is a central feature of schizophrenia.

Further, it is hypothesized that different family members will occupy different positions or roles within the family social organization, leading to differing consequences for the personality development of the offspring. This hypothesis has been confirmed by a detailed examination of very extensive material on a family in which the offspring are monozygotic quadruplet schizophrenics.

Significance to Mental Health Research:

Severely disturbed family relations have been consistently found in the background of schizophrenic reactions. This is a very important lead being examined in this project, particularly in terms of three major unsettled problems: (1) the particular characteristics of such familial disturbance in schizophrenia; (2) the degree of specificity that various aspects of such disturbance may have for schizophrenia, or varieties of schizophrenia, compared to the generality of other aspects of family disturbance which may also occur normally or in other disorders; (3) the question of whether the family disturbance is a primary factor in the development of schizophrenia or a secondary consequence of the individual's pathology.
Proposed Course of Project:

Having completed a phase of exploration of the clinical problem and the formulation of preliminary hypotheses, it is now planned to proceed with a major shift and expansion of this project, along three main lines:

(1) Comparisons of the family relations of schizophrenics with non-schizophrenics (a) initially in a time-limited (several months) pilot study with hospitalized neurotic patients and their outpatient families, (b) later, in studies of normal families, families of medical patients of other Institutes, and families of various neurotic subgroups, varied by diagnosis, social class, and family constellation.

(2) After an initial pilot comparison study with neurotics, extension of the range of observations for the families of schizophrenics both in terms of such variables as social class and family constellation, but also in terms of the variety of schizophrenia and type of onset. The question of differential effects upon schizophrenic and non-schizophrenic siblings is especially important in family studies.

(3) Extension of techniques for specifying meaningful features of both the individual psychopathology and its family setting, by trying out a variety of approaches such as group therapy with an entire family, including the patient; quasi-experimental group situations for the analysis of interpersonal communication patterns within families (see project M-P-P-(C)-9), analysis of the place of the family in the wider culture and society, and improved techniques for comparing those behavior patterns found in intra-familial interaction with those carried over into psychotherapy and the ward setting.

These changes necessarily involve other prospective changes: an enlarged patient and family sample, at first with hospitalized patients, later with others as well; a marked increase in interdisciplinary collaboration; a reorganization of the ward clinical operation.

Part B included [ ] Yes [X] No [ ]
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:


Honors and Awards relating to this project:


Partial Project Title: Perceptual Impairment in Psychogenic Mental Disorder

Principal Investigator: Lyman C. Wynne, M.D.

Other Investigators: Leslie H. Farber, M.D. and Irving M. Ryckoff, M.D.

Cooperating Units: None

Man Years (calendar year 1957): 0.2
Patient Days (calendar year 1957): 0.2

Project Description:

Objectives:

(1) To delineate the quality of an imaginative impairment in certain neurotic and psychotic patients in their ability to perceive content and create meaning. (Following general usage, perception includes, in addition to the processes of conduction and sensation, the process in which a person attributes significance or meaning to a stimulus situation.)

(2) To examine and evaluate some of the implications for personality functioning and for psychotherapeutic processes arising from this impairment. More specifically, to study the details of the imaginative impairment associated with difficulties in reading, arithmetic, and social skills, especially, how such difficulties relate to the development of anxiety, to past learning failure, and to the manner or style in which an individual brings about a sense of relatedness to others.

Methods Employed:

Research interviews were conducted with psychiatric patients and "normal" subjects, focusing on the meanings with these patients perceived with a variety of subject matter, media, and situations. Some of these interviews have dealt with the person's interpretation of particular passages which he has read, of television programs and movies and of recorded material which is played over a speaker.
Methods Employed (continued):

Others have dealt with the person's problems in dealing with common arithmetic problems and the use of maps, as occurring both in his ordinary life and in the interview situation. A session was conducted of a mother coaching her children with their reading. All of these interviews have been tape recorded and transcribed. Several have now been observed through a one-way mirror and partially photographed with sound film. Subsequently, the movies have been shown to one of the patients and her interpretation of her own appearance discussed in a further interview. Four of the patients have been also seen in psychoanalytic psychotherapy, so that information from this source could be added to the research interviews.

Patient Material:

Two inpatients (continued as outpatients in 1957) and two private patients of Drs. Farber and Ryckoff. Two "normal" mothers and their children (not patients).

Major Findings:

(1) A description has been derived of the quality of an unexpectedly extensive incapacity of these patients to perceive and deal with content, both in and out of the psychotherapeutic situation. Such massive difficulties with content may be overlooked unless specific inquiry is made in which the patient's stylistic devices do not succeed in disguising the failure to derive meaning imaginatively.

(2) In the usual situation of psychotherapy, the extent of the patient's capacity to perceive content may be obscure. The therapist is apt to believe the patient's difficulty in dealing with content arises from anxiety, instead of considering the anxiety as arising from an inability to distinguish content. In this project data are being examined which strongly suggest that an impaired capacity to perceive, understand, and communicate commonly exists independent of the impairment produced by ongoing defenses against anxiety, and frequently leads to rather than results from, anxiety. One area of functioning in which this difficulty is especially prominent is in reading difficulties of both adults and children.

(3) Not only does transference and relationship influence perceptiveness, but also, and to a greater degree, perceptiveness determines what can go into relationships. A narrow or inflexible perceptual style will markedly interfere with the development of mutuality in relationships.
Major Findings (continued):

(4) The form which the imaginative impairment takes depends greatly upon the characteristics of individual experiences in learning situations. The quality of perceptiveness and communication is markedly impaired in each psychiatric disorder and will vary in quality depending upon both the general characteristics of the disorder and the specific characteristics of the individual personality.

Significance to Mental Health Research:

It is believed that the mechanisms being studied in detail in this project plays a significant part in the learning failures widely reported in schools and by parents today, especially upon reading. In present-day psychiatric theory anxiety is widely regarded as the central problem in psychogenic mental disorders. Any evidence which challenges or calls for a modification of this viewpoint clearly is relevant to a great deal of current thinking about the nature of these disorders and their treatment. This work is an exploration of neglected dimensions in psychiatric theory.

Proposed Course of Project:

Current activity in this project is being directed toward review of past research data and writing of the material in a series of short papers each focused on a particular aspect of the work. One such paper was presented by Dr. Wynne in discussion at a meeting of the Washington Psychoanalytic Society, February 1957. It is expected that this review and writing process will continue through at least six months of the coming year. During the discussion of the material for this purpose new ideas have been emerging which it is planned to examine in further research after the writing has been done.
Part A.

Project Title: Linguistic Study of Emotional Expression

Principal Investigator: Allen T. Dittmann, Ph.D.

Other Investigators: Lyman C. Wynne, M.D.

Cooperating Units: Laboratory of Psychology

Man Years (calendar year 1957): .1

Patient Days (calendar year 1957):

- Total: .1
- Professional: .1
- Other:

Project Description:

Part A.

Project Title: Social Mobility and the Milieu of the Psychiatric Hospital

Principal Investigator: Leslie Schaffer, M.D. and Leila Calhoun Deasy, Ph.D.

Other Investigators: None

Cooperating Units: Laboratory of Socio-environmental Studies

Men Years (calendar year 1957): Patient Days (calendar year 1957):

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Project Description:

Objectives:

The study is an attempt to explore the relevance and implications of some theoretical work by Harold Lasswell concerning social structure and social mobility - particularly his notion that there is a significant negative relationship between the extent to which a group achieves solidarity and high morale and the incidence of mobility among its members. It is hoped to clarify in theoretical terms a particular perspective concerning the value context of the psychiatric hospital and, in particular, some of the problems concerning respect as a value. Among other questions one is whether there is a significant difference between the incidence and intensity of vertical mobility in a psychiatric setting as compared with conventional medical and surgical settings.

Methods Employed:

A preliminary survey of professional and other personnel in NIH and two other Institutes has been followed up by the collection of additional data in (a) a private psychoanalytic hospital and (b) a university department of psychiatry. In addition, the superintendents of two other hospitals have agreed to allow us to gather data in their institutions. Data from a random sample of 1,087 medical students has been secured through the cooperation of MORC who have promised us access to the original protocols.
Major Findings:

Statistical analysis of the preliminary data has shown a well-marked gradient of achieved vertical mobility across the professions studied. The highest degree of vertical mobility occurs in the newer professions adjacent to psychiatry—i.e., psychology and the social sciences; the least mobile population is found in physicians in internal medicine. Psychiatrists fall midway between these two groups. The further data referred to above is in the process of being collected, coded and translated on to IBM cards.

Significance to Mental Health Research:

It is suggested that some staff conflicts, both in research and in clinical psychiatric settings may be explained in terms of vertical social mobility in the participants. The notion has long been held that the provision of respect for the patient in a mental hospital is a crucial ingredient in a therapeutic milieu. It has also repeatedly been suggested that all kinds of collaborative efforts may be expected to flourish in an atmosphere of mutual respect. It has been suggested in this study that in human groups which are characterized by the participation of highly upwardly mobile persons the value of respect is implicitly conceived as a competitive value and one that is likely to be in decidedly short supply.

Proposed Course of Project:

(1) To continue to code and analyze additional data.

(2) Clarification of the theory. In a sense this study may be understood as an effort to explore the utility of a theoretical perspective elaborated by Lasswell and Kaplan for the study of political events.

(3) An abstract concerning some aspects of the work has been submitted for the 1958 Annual Meeting of the American Psychiatric Association.

Part B included Yes [X] No /
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:

Honors and Awards relating to this project:

Schaffer, L. and Deasy, L. C., "Defence, Social Mobility and Conflict in Psychiatric Settings." Presented at the Section on the Sociology of Science, American Sociological Society, August 1957, and also in a lecture given at the V. A. Hospital, Salt Lake City, Utah, September 1957. An expanded version of this paper is presently in preparation for publication.
Part A.

Project Title: Psychiatric Research in a Clinical Setting: Integrating Research and Treatment in the Role of the Clinical Investigator

Principal Investigator: Stewart E. Perry

Other Investigators: Lyman C. Wynne, M.D.

Cooperating Units: Laboratory of Socio-environmental Studies

Man Years (calendar year 1957): Patient Days (calendar year 1957):

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Project Description:

Part A.

Project Title: Selected Aspects of the Social Structure of a Clinical Research Program in the Mental Health Field: Problems Posed by the Variety of Roles Built into the Social Structure

Principal Investigator: Stewart E. Perry

Other Investigators: None

Cooperating Units: Child Research Branch

Man Years (calendar year 1957): Patient Days (calendar year 1957):

| Total: 1/6 | 40 |
|           |     |
| Professional: 1/6 |
| Other: |

Project Description:

Objectives:

To explore the consequences for a clinical research program of the variety of roles which characterize it; special emphasis will be placed on examining the problems of integrating the various administrative, research, and clinical roles and statuses.

Methods Employed:

Participant observation in a psychiatric research program; interviews with staff members; recording of group conferences, search of extant records and memoranda, research and clinical; and review of literature in medical sociology and the sociology of knowledge and science.

Major Findings:

Preliminary impressions include the following problems as consequences of the role variety in psychiatric clinical research programs: (1) There often appears to be a discrepancy between the human relations techniques emphasized in administrative roles and those emphasized in psychotherapeutic roles—for example, psychotherapeutic roles emphasize techniques of indirection in the
Major Findings (continued):

expression of views to another, while administrative techniques emphasize
directive expression of views. (2) There seems to be some discrepancy
between the pattern of integration of non-medical roles in a conventional
hospital organization and the pattern of integration of such roles in a
research operation—for example, in some instances functions performed by
doctors may be transferred to non-doctors (e.g., nurses, scientists, etc.)
and statuses ordinarily reserved to the doctor may also be occupied by
non-medical personnel. (3) Differences in the definitions of science,
method, and knowledge in psychiatry appear to be related to role differ-
ences and to engender problems in scientific communication—for example,
some research techniques are derogated or valued in relation to the staff
member's role. (4) The staff member's interpretation of crises in the
patient's hospitalization—such as suicidal attempts, acute onset of
muteness, etc.—tends to vary with his role and function.

Significance to Mental Health Research:

This project explores the operational difficulties which are inherent
in psychiatric research, treatment, and administration. Insofar as such
difficulties can be isolated and specified, it is possible that steps may
be taken to minimize their interference with organizational goals in
mental health work.

Proposed Course of Project:

Additional exploratory work is planned for the purpose of formu-
lating more explicit hypotheses and theories.
Part A.

Project Title: The Natural History of a Hospital Case Presentation

Principal Investigator: Stewart E. Perry

Other Investigators: None

Cooperating Units: None

Man Years (calendar year 1957): Patient Days (calendar year 1957):

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Project Description:

Objectives:

Taking as a starting point a hospital case presentation of a psychiatric patient, to describe the social context of the theory of behavior explicit and implicit in the case presentation; to note the potential influences of this social context upon the theory; to note the social control implications of the theoretical perspective on patient behavior which is held by ward staff; to explore the influence on patient behavior of this theoretical perspective and of the social organization of the ward.

Methods Employed:

Participant observation of the case conferences and in the general psychiatric research program; interviews with psychiatric workers who had contact with the subject patient; search of extant records on the patient.

Major Findings:

This case study indicated the following general conclusions: (1) Intellectual products (such as research reports) in a human behavior research program may be systematically studied as items of social behavior themselves. (2) A theory of patient behavior, explained psychodynamically, may offer clues to the hospital.
Major Findings (continued):

social organization within which the patient is treated. (3) Responses of personnel to a research theory may also provide clues to the hospital organization. (4) As a by-product of the study, it appeared that a review of psychiatric theory would indicate a need for explicit development of propositions about the social control of patient behavior.

Significance to Mental Health Research:

Psychiatric theories, like all theories in social science, evolve in a social context which may influence their development and their applicability; as such the theories may implicitly as well as explicitly describe the social structure of psychiatric treatment. To explore such influences and implicit descriptions is to add a further dimension to the explanation of patient behavior.

Proposed Course of Project:

This project has been terminated with the publication of a paper reporting findings in detail.

Part B included  Yes [X]  No [ ]
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:


Honors and Awards relating to this project:
NATIONAL INSTITUTE OF MENTAL HEALTH

Clinical Investigations
Child Research Branch

BUDGET SHEET

Estimated Obligations for FY 1958

Total: $443,863
Direct: $179,939
Reimbursements: $263,924

Projects included: M-CR(C) 1 through M-CR(C) 10
Project Title: Milieu Therapy

Principal Investigators: F. Redl, Ph. D., J. Noshpitz, M.D.

Other Investigators: C. Faegre, B.A., S. Crawfort, M.S.W., E. Citrin, M.S.W. J. Vernick, M.S. W., E. Maeda, O.T.R.

Cooperating Units: None

Man Years (calendar year 1957): 5 1/2
Total: 850
Professional: 3
Other: 2 1/2

Project Description:

Objectives:

Over-all Goal: To subject the various facets of milieu to an intensive as well as extensive scrutiny as to their properties and nature, and to arrive at a breakdown of this global concept into manageable and yet clinically relevant subunits. To study the precise impact of the subunits as well as the structure of the whole on the child patients as well as on the staff, to arrive at criteria for assessment of the specific psychological ingredients of milieu parts for the purpose of clinical prescription as well as prediction of milieu effects.

Sub-Tasks: Concept formation--creation of workable constructs for the differentiation of clinically relevant variables involved in milieu-effects, theory formation related to the impact of milieu-findings on the model of personality.

Pharmacopae of games and other child-patient activities--so as to create a useable manual for the prediction of their effects, and describe the variations of ingredients necessary for their adaptation to a variety of different pathologies and of different phases in treatment.

Analysis of all other milieu-aspects that can be clearly distinguished as variables in their own right, so as to make them more accessible to the process of therapeutic manipulation and to arrive at safer criteria for prediction of effects.

Methods Employed:

(1) With the aim of preparing for a pharmacopae of activity ingredients as well as of other milieu variables, a thorough analysis is being made of the records of actual in-game behavior of the child patients over an extended...
period and during different phases of their therapeutic development. Environmental stimuli involved in sub-facets of any given program or activity unit are being analysed as to their nature and potential effect on the children, and this is then compared with the actual events recorded by staff. On the basis of this analysis materials are being prepared relating to indications and counter-indications in the selection of program activities as well as for the choice of methods and techniques.

(2) The assessment of social structure, institutional atmosphere and distribution of staff roles as well as impact of staff behavior and attitudes is being pursued by a variety of methods simultaneously. The accumulation of sharply focused and detail-rich descriptions of actual situations of interaction of children and staff under varying circumstances, will still have to constitute the major method employed, since this field is as yet so poor in actual naturalistic and well described data. In isolated areas more rigorous methods are being employed on sub phases which lend themselves to such techniques, as for instance: Critical Incident technique, controlled observations by trained investigators, Ossorio-Leary system of behavioral observation, and others. On isolated hypotheses systematic analyses of historical materials and records on special incidents are pursued—such as, for instance, an analysis of the relationship between incidents reported on the child patients, and staffing patterns at the time of the incident, etc.

(3) Data from other studies are being used to define and clarify information on the impact of various aspects of the milieu on various facets of behavior. For example, CR-4 deals in part with the effects of school milieu factors on school performance, CR-5 is concerned in part with milieu effects (time, space, props, etc.) on the technique, strategy, and results of Life Space Interviews, CR-6 studies the effects of various settings on interpersonal behavior and changes in such behavior.

Findings:

This is a long range project, and major findings on the nature of the milieu concept and its clinical facets cannot be expected to emerge as yet. However, among the part-findings one could trace in the process of ongoing research the following may be listed:

(1) It is possible to isolate about 13-15 distinct and relatively independently researchable subunits of the milieu which seem to be at work in the production of behavioral impacts on the children under study.

(2) At least 7 quite distinct meanings are customarily invoked when the adjective "therapeutic" is attached to the milieu concept, each one of them relevant in its own right, but in need of sharp separation for the utilization in an organized research approach.

(3) A considerable list of properties of games, materials, props, tools involved in activities such as arts and crafts, etc., can be well isolated as of clinically distinct importance, and the therapeutic variation of these factors can be described to a considerable amount of
Part A.

M-CR(C)-1, page 3

detail. Effects of some techniques of employing such activities and of handling child behavior during the process can be distinctly seen as differing in their effect on the children from others, so that the groundwork for a more organized pharmacopoea mentioned as one of our objectives, can be seen to emerge. Such factors isolated by now can be described in sufficient detail and with sufficient precision to make them teachable to others and approachable in sharper research design in later studies.

(4) Techniques for the clinically geared observation of surface behavior on the spot can be developed and sharpened up so that they avoid the traditional gap between observable surface data on the one, and depth-psychological dynamics on the other hand more successfully than has been possible in the past.

(5) A milieu design which is well adapted to meet the children's problems in the earlier phases of their pathology, may, by this very fact, become detrimental or at least non-supportive toward later phases of recovery and on the move toward fuller mental health. The differences between the clinical characteristics of a social structure on a hospital ward as compared to that of a family style setting can be described with somewhat more detail though a really thorough analysis of residential versus institutional versus family style milieu design will have to wait for further data and explorations. Beginnings of such comparative data became possible with the move of 6 of our child patients from the Ward into the newly created Residence building, and through a trial run on a group of normal controls in that residence before the child patients were moved in.

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Major Findings:

This project is exploratory at present.

Significance to NIMH Research:

The worthwhileness of this project lies in the fact that the clinical techniques of residential therapy for use with hyperaggressive children are as yet in a developmental phase in the field of child psychiatry. The current clinical design in a number of respects is unique within the field.

Proposed Course of the Project:

This project will continue indefinitely as part of the program of the Laboratory with new areas being developed as time permits. The addition of a "Halfway House" outside the Clinical Center has already broadened the scope to include less disturbed children and later phases of treatment.

Part B included Yes X No
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:

Project Title: Studies in Psychopathology of the Hyperaggressive Child

Principal Investigators: J. Noshpitz, M. D., B. Sweet, Ph.D.

Other Investigators: H. Raush, Ph.D., H. Kitchener, M.S.W., H. Perry, A.B., P. Spielman, M.D., S. Berman, M.D., R. Lourie, M.D.

Cooperating Units: None

Man Years (calendar year 1957): Professional: 2 1/2 Other: 1 1/2

Project Description:

Objectives:

To synthesize clinical and research observations made over a long period in such a way as to formulate hypotheses about the etiology, personality assets and psychopathology of hyperaggressive children. Special attention is directed toward the testing of a hypothesis that a specific group of child patients, currently included under the label of borderline cases actually constitute a nosological entity in its own right and differ significantly from patients of the disease entities which they are usually listed as being borderline to.

Methods Employed:

1. Historical material from parents, schools, physicians, courts, social agencies, is being organized systematically toward a full developmental description.

2. Material from nursing, psychotherapy, school, social service, life space interview notes, and results from special researches are being organized and collated with each other and with biographical material, for each child.

Patient Material:

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Major Findings:

Only tentative findings can be reported at this time, since data collection on the later phases of the children's individual therapy, their behavior in the residence, as well as in public school, is still in process. However, temporary summarization has been accomplished on the material available up to the present on two of the cases, and clinical studies are in process for the other four. These studies are directed toward a synthesizing of data gained in psychotherapy as well as in the other aspects of the research project, such as previous history, school, ward and residence behavior, and so forth. Among the tentative findings the following have emerged with enough clarity to be reported at this point:

(1) Hyperaggressive children form a pathology which combines aspects from childhood neuroses and psychoses to constitute a special syndrome. Although individual children differ in aspects of this syndrome, in all cases there are profound ego disturbances centering around problems of impulse control, and particularly around the control of aggression. The ego disturbances are reflected in conceptual lacks, learning difficulties, disturbances in conceptions of space and time, low tolerance for frustration, hyperdistractibility by environmental props, readiness for contagion, paranoid-like suspiciousness and projections. Despite these features, the children being studied here differ in many features from psychotic children as described in the literature. In particular, they do not show the autistic behavior and fantasies of the latter, they are generally in communication with the environment, and under special circumstances they show marked ego-intactness.

(2) In all cases oral themes seem to play a major part in the underlying fantasies of these children. The children seem to interpret experiences via orally incorporative or destructive modes. Even material that seems initially to be predominantly phallic in tone, can be readily seen as a developmental phenomenon super-imposed on a foundation of primary oral concerns.

(3) Related to the above, one finds in these children intense anxiety over the possibility of dependency, and intense defenses erected against both behavioral and fantasy expressions of dependency. With progress these defenses seem to diminish both in behavior and in fantasy productions.

(4) All of the children show severe problems in the formation of a sense of identity. These problems seem related to the absence of or failure of figures who might serve as transmitters of cultural or subcultural values. In all cases there is absence of a father, failure of the father to fulfill a role that might provide a source for social identification, or inadequacy of the father as communicated to the child through the mother's perceptions. With all children the opportunity for establishing any relationship (even an anti-social one) with a social order seemed lacking.

Significance to NIMH Research:

Although a few detailed clinical case studies of individual children exist in the literature, this laboratory's facilities permit comparative
study of six similar children and hopefully may clarify some of the common elements seen in the personality disturbance of these children.

**Proposed Course of the Project:**

(1) Continuation of data collection of the present patient group in the residence setting, and follow up data gathering after their return home or their placement.

(2) Gathering of similar data—but with methods improved by our previous experience—on the new inpatients on 4 East, and comparison of findings on a larger number of child patients followed through several phases of their treatment.

Part B included  

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- 51 -
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:


Honors and Awards relating to this project:
Part A.

Project Title: Technical Problems in Individual Psychotherapy with Hyperaggressive Children.

Principal Investigator: B. Sweet, Ph.D., H. Kitchener, M.S.W.

Other Investigators: F. Redl, Ph.D., Ramana, Ph.D., S. Berman, M.D., R. Lourie, M.D.

Cooperating Units: None

Man Years (calendar year 1957): Professional: 1 3/4 Other: 1 1/2

Patient Days (calendar year 1957): 375

Objectives:

To define a variety of therapeutic principles and techniques which seem to be particularly indicated for hyperaggressive children within the setting of intensive individual psychotherapy. To explore a variety of therapeutic issues which arise when psychotherapy is undertaken in conjunction with intensive residential treatment; these include choice of play materials at various stages of treatment, handling of transference and counter-transference problems peculiar to this situation, the eliciting and utilization of fantasy material, the handling of various forms of resistance, etc. Problems of locating and identifying transference phenomena in the life space and communicating them to the therapist will be explored. The types of transference phenomena observable at various stages of treatment are being recorded.

Methods Employed:

In the course of seeing six children three to four interviews per week for two or more years, experiences are recorded around specific issues. For example, during the past year experience has been gained in handling various forms of resistance to coming to the therapy playroom. This has included experimenting with various policies and roles (for therapist and for life space personnel) set up to deal with this resistance.

Patient Material:

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<th>Children</th>
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<td>6</td>
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- 53 -
Major Findings:

(1) Foremost among these is the broad observation that, contrary to beliefs popular in the field, individual psychotherapy with the hyper-aggressive child is more like than unlike psychotherapy with other categories of disturbed children. As in all cases where ego development is weak or distorted, there is, especially in the early phases of treatment, greater necessity for the therapist to function as an auxiliary ego for the patient than is true in more classical neurotic cases; this, however, is no more than a difference in emphasis, since it is well known that child therapy always requires that the therapist play a partially educational role more than does adult therapy, by virtue of the fact that no child's ego is fully formed.

(2) A second impression is that the therapeutic process, while similar in course, is more prolonged than is the case with other kinds of children.

(3) Third, while limit setting plays an important role in all child therapy, it becomes particularly significant in treating children whose most crucial problems lie in the area of control, fear of loss of control, and distrust of the adult's dependability and integrity in controlling both himself and the child. Since fear of seduction (in both the narrow sexual meaning and the broader sense of seduction to impulsivity of any kind) plays a major role in the psychodynamics of these children and seductive experiences often figure prominently in their history, it becomes a vital problem for the therapist to avoid confusing the wish to demonstrate his benevolent intent with seduction. Particularly in the earlier, more disorganized phase of therapy (which may be prolonged for many months and even a year or more), it may be a disquieting experience for the therapist to find himself responded to as though he were a dangerously hostile figure, and it is easy to become unwittingly seductive in the effort to correct this projection.

(4) Many counter-transference problems also have become apparent in this project. While the particular content of the counter-transference will no doubt vary with the personality of each therapist, all those participating here have had to deal with feelings aroused by the need to meet such explosive barrages of raw destructiveness and with those aroused by the underlying oral demandingness of such children, whose own fantasy certainly seems to be one of eating up the therapist.

(5) Impressions are beginning to emerge as to specific interpretative techniques. In the earliest phases of treatment, when these children communicate largely through gross motor behavior and acting out, it seems necessary to accompany the traditional resistance interpretations with fairly concrete behavioral responses to the child; it is as though actions speak loudly while words at best mean little or, at worst, signify oral sadistic attack to this kind of child. Later, as the child moves into a phase of more symbolic communication, the interpretations also seem to need to shift; at this phase communication seems best to be achieved by corresponding symbolic gestures on the part of
the therapist, much as one answers a schizophrenic child's fantasy communications within the framework of his own fantasy rather than by interpretive translation. It seems only to be in the more advanced phases of therapy, as the child becomes able to verbalize directly about himself, that the weight of the interpretive effort can be shifted to direct discussion of the child's problems and their origins and remain effective. While all three levels of communication are present throughout therapy, there does seem to be some difference in their relative usefulness at various phases.

While it is premature to state findings about the effectiveness of therapy before it is completed, it is our impression thus far that psychotherapy is possible with such children, at least within the context of residential treatment. Issues such as the use of the ward milieu (see CR(C)-1) and the use of the life space interview (see CR(C)-5) in handling problems of therapy and resistance to therapy within a residential setting are being investigated. If impressions as to the possibilities of psychotherapy with such children were to stand up with the passage of time it would be a most significant finding in view of the widespread doubt within the field.

**Significance to NIMH Research:**

Since these children are rather infrequently given prolonged intensive psychotherapy in the community, exploratory observations of the type described above are indicated at this stage of our knowledge. Hopefully, such experiences may be helpful to other clinicians who are beginning to treat delinquents with the recently developed community support.

**Proposed Course of the Project:**

This area of inquiry is part of the on-going program of the Laboratory.

Part B included  Yes X  No.
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:


Honors and Awards relating to this project:
Project Title: Studies in Learning Disabilities in Hyperaggressive Children

Principal Investigator: R. Newman, Ph.D., S. Jacobson, M.A.

Other Investigators: J. Glaser, B.A., C. Faegre, B.A.

Cooperating Units: None

Man Years (calendar year 1957): Professional: 2  
Other: 1/2

Patient Days (calendar year 1957): Total: 2 1/2 537

Project Description:

Objectives:

To investigate the nature of the learning disturbances of hyperaggressive children and to develop techniques for their assessment as well as for their cure.

More specifically: To arrive at a sharper differential diagnosis between those disturbances of learning or school behavior which are intimately linked with the basic pathology of the children and those which are a secondary result of learning failure or behavioral learning resistances or motivational blocks.

To isolate the variables that go into making a specific learning situation ego supportive enough so that motivation for learning can develop and learning process can unfold and to isolate those variables which can be expected to be toxic or at least non-supportive to the ego tasks involved in the learning process.

To produce instruments as well as develop techniques which can be applied beyond the experimental setting and beyond the group of children on whom the study is being done.

Methods Employed:

One of the studies focused especially on (1) the problems of motivating children to maintain interest in learning projects, (2) the type of play equipment and activity choice that is needed in relation to the degree of regression or developmental lag exhibited by the child, (3) the relationship of certain specific learning deficits which appear commonly in the hyperaggressive child, such as inability or unwillingness to subtract, the fear of reading, etc., and other aspects of psychopathology,
Part A.

such as anxiety laden fantasies, etc. (4) To observe and explore the various intervention techniques needed in order to deal effectively with the child's problem in learning as well as with his behavioral manifestations during the learning process.

Besides the actual experimentation carried on with our child patients in relation to above named objectives, various sources of records were used in measurements for school participation. School records, sampled over a period of 27 months, were rated on this measure, rater reliability being checked by use of judges not connected with NIMH. Changes in the school behavior of the six children were studied by comparing ratings for two halves of the sample by time.

A modification of the Critical Incident Technique was used to develop categories of factors affecting school adjustment. School incidents for each child were classified into these categories, after rater reliability was checked.

Clinical analyses were undertaken on the learning problems of each child, and on special sources of anxiety in both children and teaching staff with respect to the learning situation.

With the new group of child patients on 4 East, methods utilized focus around the following:

1. Planned variations of school program to provide examples of behavior in different settings (individual, group; formal, informal), with different materials (verbal, manual-manipulative, etc.) and different content.

2. Participant and non-participant observation.

3. Analysis of observations to isolate variables and to develop systematic methods of describing the variables.

**Patient Material:**

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<tr>
<td>Children Male</td>
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<tr>
<td>Children Male</td>
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**Major Findings:**

1. A behavior Rating Scale, which can be used reliably in judging school incidents for adjustive behavior, was developed.

2. Over the period of 27 months the children changed significantly in the direction of better school adjustment.

3. Categories for describing clinical factors accounting for school behavior and behavioral change were developed, and it was demonstrated that they could be used reliably in judging school incidents. The clinical factors in the learning situation can be subsumed under three major categories:
Part A.

1. Self (self picture; inner pressures and forces; infantile needs and frustrations)

2. Relationships (to adults; to peers)

3. School (subject matter, methods, material; teacher personality)

Patient Material:  

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<td>Children Male</td>
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Significance to NIMH Research:

1. The instruments developed here can be used in other studies of learning disturbances with other groups of children.

2. The juxtaposition of a therapeutic school program to intensive residential treatment and psychotherapy is perhaps unique in the field and presents unusual opportunities for sifting out those therapeutic issues which are best dealt with in school and those which are common to all three settings.

Proposed Course of the Project:

Further investigation, refinement, and broadening of these methods, their collation with other data from school and from other sources.
PHS-NIH
Individual Project Report
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Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:

Honors and Awards relating to this project:

Project Title: Studies in Life Space Interview Strategy and Techniques

Principal Investigator: F. Redl, Ph.D., H. Kitchener, M.S.W.

Other Investigators: A.T. Dittmann, Ph.D., J. Noshpitz, M.D., H.L. Raush, Ph.D., P.M. Spielman, M.D., J. Vernick, M.S.W.

Cooperating Units: None

Man Years (calendar year 1957): Total 1 3/4
Professional 1 1/4
Other 1/2

Patient Days (calendar year 1957): 420

Project Description:

Objectives:

Psychiatric In-Patient treatment of children necessitates the use of interview techniques not only during specifically designed Therapy Sessions of the child with his doctor, it becomes important to add interviews carried on by other adults in the hospital or residential setting, in high proximity to the events of the day.

We designated this type of interview by the term Life Space Interview and approached our study of this technique with the following objectives in mind:

(1) To explore the variety of situations that suggest the use of Life Space Interviewing as a therapeutic measure.

(2) To subject the technical problems that emerge in this type of work to an organized scrutiny as to the impact of the setting, the issue, the objectives of a given intervention, the specific pathology of the child as well as other factors in the surrounding milieu.

(3) To collect well recorded illustrative samples for all those aspects from the sum total of life space interviews recorded, and to

(4) Work toward a well documented technique of Life Space Interviewing similar to the rigorous concept of technique that has been developed over the years in the more well known style of psychiatric interview therapy in the office setting.

Methods employed:

Over 500 records of Life Space Interviews at varying phases of the
therapy of our child patients have been gathered. Some of these have been recorded post-situationally by the interviewer, others have been recorded by means of stimulated recall--the interviewer reporting to a trained researcher following the episode.

Through individual exploration and group discussion of these materials categories have been devised which shall be used as basis for the coding of interview materials, and part of the material has been coded.

Using interview notes, a preliminary empirical analysis was made comparing interviewer techniques in Life Space Interviews with interviewer techniques in Play Therapy Interviews. Interviewer techniques were coded into 25 categories under seven major headings.

Data collection as well as conceptual exploitation of the data so far gained for the development of a theory and technique of the Life Space Interview has been continued in both settings, the Ward as well as the Residence.

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Major Findings:

Among the preliminary findings, presented at the National Conference for Orthopsychiatry in 1957 are the following:

1. The variety of purposes for which treatment staff uses Life Space Interview techniques can be ordered around the following sub-goals which seem to emerge most frequently in in-patient treatment of children with aggressive disturbances:

A) Clinical Exploitation of Life Events, under which categories distinct from each other are temporarily singled out under the following labels: (1) reality-rub-in, (2) symptom estrangement, (3) revitalization of numb value areas, (4) new tool interpretation, (5) manipulation of the boundaries of the self.

B) Emotional First Aid on the Spot with subcategories temporarily classified under the following code labels: (1) drain-off of frustration annoyance (2) communication maintenance in moments of relationship decay, (3) support for the management of panic, fury and guilt, (4) regulation of behavioral and social traffic, (5) umpire functions in decision crises and in cases of loaded transactions.

2. In terms of exploration of Criteria for the indications or counterindications of holding Life Space Interviews in a given situation, and of the choice of a specific technique, the following 6 sub-categories of areas of major relevance have emerged: (1) central theme-relevance, (2) ego proximity and issue clarity, (3) role compatability, (4) mood manageability, (5) timing (6) impact of terrain and props.
(3) On the basis of preliminary work a number of similarities were found between techniques employed by interviewer in Life Space and in Play Therapy Interviews. Among the differences in the techniques employed in the two types of interviews were the following: (1) as expected, play is used less frequently by Life Space Interviewers; (2) techniques of control were used more frequently by Life Space Interviewers; (3) while there were no differences in the amount or specific techniques of interpretation used in the two types of interviews, there were differences in the direction of interpretation: In Play Therapy Interviews interpretations were directed more frequently toward impulse, whereas in Life Space Interviews interpretations aimed relatively more frequently toward resistance and defense.

All these findings are based on the first few years with our special group of child patients and in the earlier phases of their individual and milieu therapy. Expansion of data collection as well as concept-reformulation is of course contemplated before more final conclusions can be drawn. The abundance of rather untraditional terminology for labelling our temporary findings and categories must be understood out of the fact that this is quite a new field of exploration, and that more static technical terminology has not yet been developed. In part, it also constitutes the conviction on the side of the investigators that a premature forcing of newly emerging concepts into all too rigidly technical terms might lead into a premature theory-freeze which we are eager to avoid.

**Significance to NIMH Research:**

The life space interview is a relatively unexplored psychotherapeutic technique which holds considerable promise for future employment in treatment institutions if it can be further developed.

**Proposed Course of the Project:**

This is a continued project.

Part B included

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- 63 =
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Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:


Honors and Awards relating to this project:
Part A.

Project Title: Studies of Change in Hyperaggressive Children During the Course of Residential Treatment

Principal Investigator: H. Raush, Ph.D

Other Investigators: F. Redl, Ph.D., S. Sweet, Ph.D., T. Taylor, M.A., A. Dittmann, Ph.D.

Cooperating Units: None

Man Years (calendar year 1957): Professional: 1 1/2 170
Total: 2 1/2
Other: 1

Project Description:

Objectives:

(1) To develop concepts of improvement that are clinically relevant and sophisticated, but go beyond the listing of dropped out pathology. We hope to arrive at descriptions of the functioning of the intact ego and of other personality characteristics commonly associated with a state of Mental Health. We aim at descriptions as specific and as sharply focused as concepts for the description of pathology.

(2) To develop methods for the assessment of change in behavior patterns of children in a wide variety of aspects as well as settings and situations such as children would be expected to be exposed to in in-patient residential therapy.

(3) To develop criteria for the differentiation of change in general, as compared to the assessment of therapeutic movement as a result of exposure to treatment, and

(4) Assess the actual changes that occurred in these particular child patients during the various phases of their therapy.

Methods Employed:

(1) Existing recordings of all phases of the patient's therapy and life experiences were studied and compared in order to find where traceable patterns of change can be seen to emerge.

(2) A series of studies was undertaken with the special purpose of focusing on various aspects of change:
(a) Systematic observations in a variety of settings and coding of individual interactive behavior during two treatment phases.

(b) Systematic observations done on a control group of children, matched for age, IQ, race, socio-economic status.

(c) Categorization derived from detailed descriptions contained in clinical records and case conference materials.

(d) Periodic interviews and collections of clinical incidents from Child Care Staff.

(e) Exploratory interviews with child care and therapy staff directed at staff's concept of change and improvement and matched with their actual statements about observed functioning of their patients.

**Patient Material:**

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<td>365</td>
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<td>Children Male (control)</td>
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**Major Findings:**

(1) Changes in behavior interaction patterns. From the investigation of two series of observations made a year and a half apart, the following major conclusions can be drawn:

(a) The interpersonal behavior of the children has changed considerably in the course of treatment.

(b) Over the period there is a decrease in inappropriate behavior toward peers. Most children show a trend toward more friendly peer relationships.

(c) Changes in relations with adults are much more marked than changes in relations with peers. Hostility toward adults decreases considerably. Particularly, there is a decline in hostile-dominant behavior and an increase in friendly-passive behavior toward adults, with a major increase in trusting, dependent expressions. Inappropriate behavior also decreases considerably. The distinction between behavior toward peers and behavior toward adults gets sharpened.

(d) The behavior that the children evoke from others shows corresponding changes. Children are less hostile than they were in response to a particular child. Adults show an increase in the proportion of friendly, giving, supportive behavior with the children.

(e) Different behavioral settings produce different qualities of interpersonal behavior.

(f) There is an interaction between person and situation that goes
Part A.

beyond what either contribute independently to our ability to predict behavior. That is, although there are generalizations, settings also operate differentially for different children.

(g) The effects of settings differ in the two phases. Tentatively, it would seem that in the later phase of treatment the situation comes to play a greater role as a determinant of behavior than it did previously.

(h) Changes in interpersonal behavior appear more readily in some settings than in others.

(i) A paper on some of these findings was presented at national meetings and is in process of publication. Data analysis is near completion and another paper is being worked on.

(2) Concepts of Improvement.

(a) Formulations of a sharpened up and clinically relevant concept of improvement are undergoing continuous change as our study proceeds, and temporary findings are as yet too volatile to be reported this year.

(b) A pilot study for the collection of data on the staff's concept of improvement as related to our present child patients is in a state of partial completion. Preliminary impressions from the data indicated that the children have improved in a number of areas. Especially, hostile interactions between children have decreased and acceptance by the children of staff interventions has gone up. Other details about improvements are too varied from child to child or require too much background data to be summarized here.

Significance to NIMH Research:

With some modification findings and methods should be applicable to other settings: Adult psychiatric in-patient settings, school situations, etc. The area of change and improvement is critical for psychiatric and psychological research in general.

Proposed Course of Project:

(1) Completion and write-up.

(2) Completion of coding and analysis of control data; further observations of patient group in new residence.

(3) Completion of paper.

(4) Further work toward development of categorization scheme.

Part B included  Yes  No  X
Part A.

Project Title: Interaction Patterns of Normal and Hyperaggressive Children

Principal Investigator: Allen T. Dittmann, Ph.D. (Psychology), D.W. Goodrich, M.D. (Psychology)

Other Investigators: None

Cooperating Units: None

Man Years (calendar year 1957): None

Patient Days (calendar year 1957): None

Project Description:

Objectives:

(a) To develop methods of studying interaction patterns of children in a treatment ward. (b) to compare interaction patterns of normal and disturbed children in the same setting.

Methods Employed:

Short sample observations were taken of groups of children in specific situations on the ward and in the field, situations selected for their conduciveness to nurturing and limit-setting adult behavior. Observations were recorded on tape by intensive interviewing of the observer: the recordings form the basic data of the research. These protocols were coded for interactions between children and interactions involving children and adults.

Patient Material:

None this year.

Major Findings:

Patterns of interaction of the two groups showed differences such as might be expected: Less inappropriate behavior, less overt aggression among the normals, more real leadership; greater dependency based on trust toward adults. Adult behavior toward the children includes greater freedom with the normals in expressing affection setting limits, while with the disturbed children adults are more caution in their expressions.

Significance to NIMH Research:

The method can be used in descriptive studies where group differences
Part A.  

are the focus. The method's disadvantages were clearly shown by the experience of this study: Recalling everything that goes on with six children in even a very short observation is impossible, even with intensive interviewing of the observer. Since the data for this study were collected the observational method has been refined to get more complete information on one child in one observation, so that sequences of interaction can be followed. See M-CR(C)-6.

Proposed Course of Project:

A paper is in preparation.

Part B included  Yes  No X
Serial No. M-CR(C)-8
1. Child Research Branch
2.
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
Calendar Year 1957

Part A.

Project Title: Research on Anger in Interpersonal Situations

Principal Investigator: D. Kaplan, M.S.W. (resigned 9/21/56).
D.W. Goodrich, M.D. (Psychology).

Other Investigators: T. Taylor, M.A., F. Redl, Ph.D.

Cooperating Units: None

Man Years (calendar year 1957): None
Patient Days (calendar year 1957): None

Project Description:

Objectives:

To explore descriptive concepts for analysis of anger episodes in interpersonal situations within this residential treatment center. This study proposed to develop a theoretical model including categories to describe the various phases of an anger episode.

Methods Employed:

Approximately 300 anger episodes have been collected by non-participant and participant observers. A preliminary analysis of these has led to development of a model for the anger sequence in interpersonal situations.

Patient Material:

None this year

Major Findings:

With the aim of developing a schema for the analysis of provocative techniques used in anger episodes, some 50 incidents were examined in detail, and preliminary attempts at codings were made. A total of 15 over-all headings and 53 sub-categories of provocative techniques were described, and examples were given.

Significance to NIMH Research:

One of the major forms which symptomatology takes in hyperaggressive children is outbursts of aggression against others. By means of this study
Part A.

an important aspect of the psychopathology of many delinquent children may be clarified.

Proposed Course of the Project:

A paper has been published and the project is discontinued.

Part B included Yes X No.
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:


Honors and Awards relating to this project:
Part A.

Project Title: Staff Values Concerning Therapeutic Interventions with Hyperaggressive Children.

Principal Investigators: D. S. Boomer, Ph.D. (transferred to Laboratory of Psychology), D. W. Goodrich, M. D. (Psychology)

Other Investigators: None

Cooperating Units: None

Man Years (calendar year 1957): 0

Patient Days (calendar year 1957): 0

Project Description:

Objectives:

To survey the matrix of common assumptions and therapeutic values which underlie the therapeutic behavior of the staff of Children's Unit, NIMH. To formulate these generalizations in such a way as to maximize their usefulness for research and training.

Methods Employed:

The technique utilized was the so-called "critical incident" method. Each staff member was regularly interviewed by one of the investigators over a 3-month period, to elicit accounts of actual therapeutic interventions with children, engaged in or witnessed by the staff member. The incidents thus collected were then categorized with regard to natural dimensions which emerged from the data.

Patient Material:

No. Average Stay (Days)

None this year

Major Findings:

Approximately 240 critical incidents were collected and categorized. The final groupings are 38 in number, distributed among four superordinate headings:

A. Promoting personality change by helping child to learn to view his own behavior evaluatively.

B. Promoting ego growth.
C. Supporting existing ego controls.

D. Managing one's own conduct as a staff person.

An interim report has been prepared presenting these categories together with a selection of critical incidents illustrative of each. A paper was presented at the American Orthopsychiatric Association.

Significance to NIMH Research:

(1) The clinical staff of the Children's Service has been furnished with our findings to make use of as they see fit, in research, or training of new personnel.

(2) Our method has been demonstrated, and shared with other NIMH investigators. This method, adapted from an industrial psychology tool, seems to be a useful way of formulating concepts concerning a complicated clinical operation.

Proposed Course of the Project:

Publication of material.
Project Title: A Study of Behavior Reporting by Child Care Workers

Principal Investigators: B. Iflund, Ph.D., D. W. Goodrich, M.D. (Psychology)

Other Investigators: None

Cooperating Units: None

Man Years (calendar year 1957): 0

Patient Days (calendar year 1957): 0

Project Description:

Objectives:

To determine (1) the consensus of expectations by the staff concerning what should be included in the daily descriptive notes made by counselors on patients' overt behavior; (2) the extent to which such expectations are met subjectively; and (3) the extent to which these notes in reality actually achieve these expectations.

Methods Employed:

Eleven child care workers and twelve clinicians ranked seventeen categories of items whose frequency of occurrence in a large sample of behavior notes had actually been determined. Rankings were obtained which revealed the subjective judgment of the child care workers and clinicians concerning what is contained within the notes as well as rankings which reflect what would be most desirable to be in the notes. A comparison between what is expected and what is believed to be present was used as a measure of satisfaction or dissatisfaction. Since actual frequencies are also available one can determine further the extent of awareness of what is in the notes on the part of those reading them (the clinicians) and those writing them (the child care workers).

Patient Material:

None this year

Average Stay (Days)

Major Findings:

Tests of concordance within each group showed the amount of agreement to be significant at better than the .01 level. Thus we are justified in considering the combined results of each group.
Correlations were determined between the following variables: Actual rank order of frequency, the clinician's "Ideal" order, child care workers' "ideal" order, clinicians' concept of what is in the notes, and child care workers' concept of what is in the notes. Eight of the ten correlations carried out were significant.

Factor analysis of the above correlations yielded two factors which account for the major portion of the variance. One of the factors is defined by the clinician's ideal; the other factor by both what the clinicians and child care workers think is actually present. In reality the notes themselves have equal loadings of both factors.

Significance to NIMH Research:

The statistically significant results obtained seem to suggest that further studies of the perception of adults in this setting may be profitably carried out in relation to the behavior reports of the staff.

Proposed Course of the Project:

Publication of the paper

Part B included Yes X No
Clinical Investigations
Laboratory of Psychology--Section of the Chief

BUDGET SHEET

Estimated Obligations for FY 1958

Total: $250,971

Direct: $110,941

Reimbursements: $140,030

Projects included: M-P-C(C) 1 through M-P-C(C) 13
Part A.

Project Title: Administration of Laboratory of Psychology
(A Joint Operation of the Clinical Investigations and Basic Research Programs)

Principal Investigator: David Shakow

Other Investigators: None

Cooperating Units: None

Man Years: 
  Total: 1.70
  Professional: .70
  Other: 1.00

Patient Days: none

Project Description:

Objectives: A. To achieve an administrative structure which will provide the optimum of communication with (1) Chief of the Laboratory, (2) among members of a section, (3) within the Laboratory as a whole, (4) and with other investigators and units in NIMH and other Institutes, and at the same time result in the least interference with the objectives and time for research of individual investigators.

B. To complete organization of Laboratory.

Methods Employed: A. To achieve optimal administrative structure: Organization into a reasonable number of sections, conduct individual conferences with investigators, hold the minimal necessary number of meetings with individual section chiefs and with the group of Section Chiefs in the Laboratory as a whole.

B. To complete the organization: Recruitment of additional personnel.
Part A: Project Description (Cont'd)

Major Findings:

1. Personnel by Sections (Professional):

   **Clinical Investigations Program**

   Section of the Chief
   Shakow, David (Chief)
   *Bergman, Paul
   Dittmann, Allen
   Kendig, Isabelle
   Rosenthal, David
   *Zahn, Theodore

   Section on Child Development
   Bayley, Nancy (Chief)
   Bell, Richard Q.
   Gewirtz, Jacob L.
   Rheingold, Harriet
   Schaefer, Earl S.

   Section on Personality
   Parloff, Morris (Acting Chief)
   Boomer, Donald
   *Handlon, Joseph
   **Kelman, Herbert
   *Waldman, Marvin

   **Basic Research Program**

   Section on Aging
   Birren, James (Chief)
   Bondareff, William
   Botwinick, Jack
   Jerome, Edward A.
   Streicher, Eugene
   Weiss, Alfred

   *Kay, Harry (Visiting Scientist)

   Section on Animal Behavior
   Rosvold, H. Enger (Chief)
   Mishkin, Mortimer
   Mirsky, Allen

   *Bättig, Karl (Visiting Scientist)
   *Bush, Elinore (NIMH Fellow)
Part A: Project Description (Cont'd)

Major Findings (Cont'd)

2. Program of conferences held by Chief of Laboratory

3. New Section -- Limbic Integration -- jointly with Laboratory of Neurophysiology, was organized with Dr. Paul MacLean as Chief.

Proposed Course of the Project:

1. Continuation of attempt to recruit Section Chiefs for Section on Personality, and Perception and Learning. Although for the Section on Perception and Learning serious negotiations were under way last spring and summer with a very prominent psychologist for this position, his decision was finally in the negative because of space limitations -- we could offer him so much less than he already had in his university laboratory. We appear now to be more fortunate in relation to the Chiefship of the Section on Personality. Negotiations are under way with a very promising person and it seems likely that we shall be able to make the final arrangements early next year for a reporting date sometime during the summer of 1958.

2. Because of certain present limitations in our own Clinical Center facilities, in some areas of our research, notably Child Development, it has been necessary to attempt to find settings outside this building. Some arrangements have already been made and others are in process of being made to find satisfactory settings in the Washington area for carrying out the planned researches. The hope is that the Clinical Center will eventually be able to furnish some of these facilities.

3. The coming year should see more involvement of the members of the Laboratory in collaborative projects with the Adult Psychiatry Branch, the Laboratory of Clinical Science, and the Clinical Neuropharmacological Research Center at St. Elizabeth's.
Part A.

Project Title: The Analysis of the Psychotherapeutic Process: The cumulative information derived from repeated viewing of complex material.

Principal Investigator: David Shakow

Other Investigators: None

Cooperating Units: None

Man Years: Patient Days: None
Total: 1.0
Professional: 1.0
Other: .0

Project Description:

Objectives: To determine what additional relevant information necessary for the understanding of the therapeutic process is derived from successive viewings of a film of a psychotherapy session, and whether there are major differences between active and passive analytic approaches to data of this type. (Such a study is important because a major problem arises as to how complex data of this kind best lends itself to significant analysis.)

Methods Employed: The film for one psychotherapeutic session is divided into four sections. Each section is viewed repeatedly (15 times) under one of four sets of conditions: active attitude/once per day; active attitudes/all 15 in one day successively; passive, free-floating attention/once per day; passive free-floating attention/all 15 in one day successively. This pilot experiment is being carried out as a preparation for determining the design of the analytic process to be followed in the major project on the analysis of the therapeutic process. The experimenter dictates into a recorder as much as he can
Part A (Cont'd)

Methods Employed (Cont'd)

both during the running of the film and immediately afterwards with regard to content process, relationship, cues for all of these, etc., and a comparison is subsequently made of the kinds of material which is added at successive viewings.

Major Findings: No findings as yet. The study is in its early stages. Apparatus problems developed which limited the amount of data collected.

Significance to the Program of Mental Health Research: This is one of a series of studies directed at solving certain methodological problems in carrying out research in the field of psychotherapy. The importance of this general area for research is considered in Project Description Sheet M-D-(C) 1, titled, "The Analysis of the Psychotherapeutic Process, particularly the Psychoanalytic Process."

Proposed Course of Project: Depending upon the results from the completion of the first experiment, further experiments will be set up with additional subjects and with more rigorous design and categorizations. The acquisition of a new projector should make possible the prosecution of this project with greater facility.

Part B included: No
Part A.

Project Title: Psychology of Schizophrenia

Principal Investigator: David Shakow

Other Investigators: David Rosenthal, Theodore Zahn, Joseph Handlon, Marvin Waldman

Cooperating Units: None

Man Years:  
Total: 1.5  
Professional: .5  
Other: 1.0

Patient Days: None

Project Description:

Objectives: To bring together a large body of experimental data on schizophrenia collected over many years into a series of monographs developing a theory of the psychology of schizophrenia. A detailed analysis of the body of experimental data already available and of new data to be gathered on our wards here and at St. Elizabeth's (see Project Description M-P-C-(C) ) will be carried out to test certain hypotheses as to the importance of difficulties during the period of preparation for response in schizophrenics.

Methods Employed: In relation to the already accumulated material, ranging in complexity from studies of the latent time of the patellar tendon reflex to studies of social response, the usual methods of statistical analysis will be utilized. Some new developments deriving from studies of Phillips, Rodnick and Garmezy regarding good and poor prognosis, and certain other studies on "reactive" as opposed to "process" schizophrenics will be utilized for further differentiation of the material. Several related studies are being carried out on senescent and brain damaged subjects and they will be used in this study for control purposes.

Patient Material: For this particular study no patient material will be required. The data are already collected.
Part A (Cont'd)

Major Findings: Some of the major findings from this material have already been reported by the proponent and his former colleagues in an extensive series of papers on the psychology of schizophrenia. The present project is directed at working up as yet unpublished material and reworking the total material in the context of a more carefully delineated theory.

Significance to Mental Health Research: Despite the fact that schizophrenia is the major disease group of mental disorders and accounts for half the occupied beds in mental hospitals, little advance has been made in dealing with this problem. A major defect undoubtedly has been in the relatively unestablished theories proposed to account for this complex of disorders. It is hoped that the proposed study will contribute to an understanding of the underlying factors.

Proposed Course of Project: Continuation of analysis of material and tying it in with experimental findings of current experimental studies.

Part B Included: No.
Part A.

Project Title: Linguistic Study of Emotional Expression

Principal Investigator: Allen T. Dittmann

Other Investigators: Lyman C. Wynne

Cooperating Units: Adult Psychiatry Branch

Man Years (calendar year 1957): Patient Days (calendar year 1957):

Total: .4
Professional: .2
Other: .2

Project Description:

Objectives: This project is an attempt to find ways of coding speech in order to identify disturbances which may be used as an index for psychological disturbance.

Methods Employed: Techniques of linguistic analysis developed by Trager and Smith as applied to psychotherapeutic interviews.

Major Findings: (a) Pitch, stress and juncture patterns. These can be coded with high reliability, but do not in themselves relate to outside judgments of disturbance. Judgments of inappropriateness of juncture patterns could be related to disturbance, but the relationship was not strong enough to make this a useful source for individual prediction. Subsequent attempts to make judgments of appropriateness of entire phrases based on the configuration of pitch, stress, juncture all taken together, proved not to be related to disturbance. This finding leads us to believe that the meager positive results from appropriateness of juncture patterns alone were the result of capitalization on chance. Our conclusion is that these microlinguistic phenomena are too closely related to the syntax of language to be carriers of emotional communications.

(b) Hesitations and "breaks" in speech. These can be coded with fairly high reliability, but psychological states other than disturbance or anxiety affect these phenomena. It is impossible to differentiate, for example, between anxiety and meditative reflection using these codings. It may be that other systems, based partly on content, will do this job...
better. See, for example, the project, "Development of an Ego-Integration Conceptual System for Studying Psychotherapy", of Goodrich and Boomer in the Section on Personality of this laboratory.

(c) During the year of this report we have been trying to develop in a more systematic way the vocal phenomena of speech other than those mentioned above, the "paralinguistic" phenomena. These include changes in duration, loudness, pitch, intensity, articulation, and vocalization as applied to units of speech larger than the morpheme. Preliminary trials indicate that the paralinguistic phenomena can be coded fairly rapidly, and that a good deal of work is necessary to spell out the criteria for coding completely enough that objective measurements can be made.

**Significance of the program to Mental Health research:** This project is part of the program devoted to determining ways of measuring non-verbal communication channels. If successful, it will sharpen our ability to use interview data more completely in the analysis of psychotherapy.

**Proposed course of the project:** To continue the development of these techniques until we find that we have objective measurement techniques or that linguistic techniques are not the way to get at vocal communicative phenomena.

Part A. Project Description Sheet (cont'd.)

Part B included [ ] Yes [x] No [ ]
Project Title: Judgment of facial expression from short sequences of motion picture film

Principal Investigator: Allen T. Dittmann

Other Investigators: none

Cooperating Units: none

Man Years (calendar year 1957): 1.2
Patient Days (calendar year 1957): 1.2

Professional: .6
Other: .6

Project Description:

Objectives: To develop techniques of judging emotion from motion pictures so that these may be used for sequence analysis of therapeutic interviews. This project is related to Linguistic Study of Emotional Expression.

Methods Employed: During the year of this report the technique of showing short series of prints from motion pictures was abandoned as being artificial, even though it was a far simpler method of presenting data to judges than the one finally evolved. The present technique involves showing short sequences of film through a motion picture projector to judges, sequences about three seconds in length. Judges make their responses by checking a list of 17 categories of emotional tone, and final scores are derived from this list. Reliability of pooled scores of three independent judges was .85 for 24 items.

A pilot study was run to test whether these scores could be related to other variables. Using sequences of film of a patient following leading responses and confrontations by the therapist in one interview, judgments of facial expression showed greater relatedness and calm following leading responses and greater discomfort and apprehension following confrontations. Judgments based on speech with meaning filtered out and on content alone showed trends in the same direction, but the relative unreliability of these judgments for these data meant that the differences were not significant.
Part A. (Project Description Sheet cont'd.)

Major findings: This technique definitely holds promise as a method of getting at emotional communication as mediated by visual cues. Reliability on a very limited sample is high, and the judgments can be related to other variables.

Significance of the program to the Institute: Here is a technique for measuring nonverbal communication which appears to work. While it is not simple to carry out (motion pictures must be used as the basis for judgment), this method, or rather those which are developed from it, may find wide use in analysis of interviews and other situations where films are available.

Proposed course of the project: The preliminary findings are based on very limited material, and further work is under way enlarging the scope to include many patients in many different stages of psychotherapy. At each stage in the development, reliability tests will be run, and pilot studies similar to the one cited above carried out.

Part B included  Yes [ ] No [X]
Part A.

Project Title: Interaction patterns of Normal and Hyperaggressive Children

Principal Investigator: Allen T. Dittmann

Other Investigators: D. Wells Goodrich

Cooperating Units: Child Research Branch

Man Years (calendar year 1957): Patient Days (calendar year 1957):

Total: .3
Professional: .2
Other: .1

Project Description:

Objectives: (a) To develop methods of studying interaction patterns of children in a treatment setting. (b) To compare interaction patterns of normal and disturbed children in the same setting.

Methods Employed: Short sample observations of children in situations selected to represent daily life experiences. Observations were recorded, and the recordings formed the basic data of the research. Protocols were coded for interactions between children and interactions involving children and adults.

Patient Material: None during the year covered by this report.

Major Findings: Patterns of interaction of the normal and hyperaggressive children differed as might be expected: normals showed less inappropriate behavior, less overt aggression, more real leadership, greater dependency based on trust toward adults. Adult behavior was not so clearly expected: more freedom with normals in expressing affection, setting limits, while with the disturbed children they were more cautious in all their expressions. Extensive studies of reliability of the observational method itself and of the coding system used here showed that the methods were repeatable by the same people at different times and by different people at the same time, thus
Part A. Project Description Sheet (cont'd.)

lending greater credibility to the findings. During the year covered by this report the work has been chiefly concerned with reliability studies.

The initial methodological paper is complete, and the substantive findings are in the process of being written.

Part B included       Yes ☐ No ☒
Part A.

Project Title: Studies of dimensionality of psychological variables

Principal Investigator: Allen T. Dittmann

Other Investigators: None

Cooperating Units: None

Man Years (calendar year 1957): 0.5
Professional: 0.1
Other: 0.4

Project Description:

Objectives: To investigate systems of psychological variables for their dimensional structure, using non-metric techniques.

Methods employed: Methods developed by W. L. Hays and the late J. E. Bennett under the general theory of C. Coombs are used. Systems investigated are the Freedman-Leary-Ossorio system of Interpersonal Mechanisms and the Schaefer Circumplex of child-rearing attitudes. Leary has concluded that the Interpersonal Mechanisms form a two-dimensional scheme, and has applied plan trigonometric manipulations of individual profiles based on the system to handle group data. Schaefer has said that the behaviors concomitant with child-rearing attitudes can be cast in two dimensions, and finds similarities with the dimensions proposed by Leary.

Major Findings: Non-metric analysis of these two systems shows that at least three dimensions must be posited to account for the behaviors which they purport to organize into only two dimensions. The end-points of these dimensions have not been worked out as yet, but the indications of preliminary work are that they do not coincide with those suggested by the authors of the systems.

Significance of the program to Mental Health research: The system of interpersonal mechanisms is in use in two studies in
Part A. Project Description Sheet (cont'd.)

the institute (in the Laboratory of Socio-Environmental Studies and the Child Research Branch), and theoretical analysis of its properties will give information on how it may be most profitably used and on what are its limitations. The Schaefer circumplex will be used in organizing data of a different kind in the Section on Child Development, and can also profit from data from a number of different kinds.

Proposed course of the project: To complete the analysis in order to find end-points of the dimensions, and to publish the results.

Part B included Yes [ ] No [X]
Part A.

Project Title: The Self-concept and Body Image as Related to Disease Susceptibility and Organ Choice

Principal Investigator: Isabelle V. Kendig

Other Investigators: None

Cooperating Units: National Institute of Arthritis and Metabolic Diseases

Patient Days (calendar year 1957): 6

Professional: .53

Other: .05

Project Description:

Objectives: To explore attitudinal factors affecting health and longevity. More specifically, to investigate those attitudes inculcated in early childhood which are instrumental in determining the nature of the self-concept and the body image especially in relation to susceptibility to illness, organ choice, course and outcome of disease.

Methods Employed: Extensive use of self-concept tests and a variety of projective techniques, including the Rorschach, Draw-a-Person and Four Picture tests, with patients proved unsatisfactory, the results reflecting only the present self-concept and body image as unfavorably modified by years of illness. It seemed necessary, therefore, to develop a detailed questionnaire or interview schedule which would disclose the attitudes toward the self and the body inculcated in early childhood, explicitly by direct instruction and implicitly through the emotional climate of the home and family reactions to illness, which might bear a relation to subsequent disease susceptibility. During the past year such an instrument has been developed and pretested on two patient groups and one group of 'normal' controls. Scales are now being drawn so that the data can be coded and treated quantitatively.
Part A. Project Description Sheet (cont'd.)

Patient Material: The two patient groups used for pre-testing the interview schedule have consisted of a number of rheumatoid arthritics from NIAMD and a smaller number of patients from NINDB referred for study because of intractable pain. In addition, the instrument has been administered to 'normal' controls involved in drug studies.

Major Findings: There are no substantive findings to report at this time as the emphasis to date has been upon the development of an appropriate methodology.

Significance of the program to Mental Health research: To the extent to which the results of this study may throw light on the part which beliefs and attitudes to the self and to the body play in relation to subsequent health and to longevity, it should have value in forwarding the work of the various Institutes in which it is carried on. It should also tie in with studies in progress in the Laboratory of Psychology, specifically in the fields of child development and gerontology. In these areas it will be significant to trace the rise, modification and deterioration of the self-concept over time in its effect upon resistance to disease.

Proposed Course of Project: Before the close of the current year it is expected that the coding of the Interview Schedule, which has already passed through a number of forms, will be completed and a weighted scoring system devised. It will then be used with groups of patients in NCI, NHI and NIAID as well as in NIAMD and NINDB. The next step will be to secure matched control groups, the Peace Church 'normals' being largely unsuitable because of the age factor.

A subsidiary project has been in the ways since spring, viz. to compare the physical status of a group of Principia College students, raised in the Christian Science faith, with a matched group of students from a denominational college of similar standing, to all of whom medical examinations were given by a Navy team during the Second World War. Permission for access to the reports on these examinations has already been granted by the Navy and the project is now under consideration by the Christian Science Mother Church in Boston. This study should afford a crucial test of the extent to which affirmative attitudes to health inculcated in childhood contribute to subsequent resistance to disease.

Part B included Yes [ ] No [ ]
Part A.

Project Title: Precocious Puberty and Pseudohermaphroditism

Principal Investigator: Roy Hertz, M. D.

Other Investigators: Isabelle V. Kendig

Cooperating Units: National Cancer Institute

Man Years (calendar year 1957): 3

Patient Days (calendar year 1957):

- Total: .08
- Professional: .03
- Other: .05

Project Description:

Objectives: From the standpoint of the second investigator, the objective of this study is to evaluate the psychological effects of precocious puberty and pseudohermaphroditism on personality variables, particularly upon the self concept and the body image.

Methods Employed: Administration and analysis of the standard intelligence and projective tests.

Patient Material: All present out-patients and all newly admitted patients to the NCI suffering from precocious puberty and pseudohermaphroditism, an estimated 15 a year.

Major Findings: The group of patients seen to date (5) is still too small to warrant any statement in re findings.

Significance of the program to Mental Health research: Besides throwing light on general personality variables in such a group of patients, the study should contribute significantly to our understanding of the bearing of such pathology on the self concept and the body image.
Part A. Project Description Sheet (cont'd.)

Proposed Course of Project: To continue to see new patients with these diagnoses and to re-evaluate from time to time those already seen until an n is built up of sufficient size to warrant conclusions about the group as a whole.

Part B included Yes ☐ No ☒
Part A.

Project Title: Study of Intractable Pain

Principal Investigator: John M. Van Buren, M.D.

Other Investigators: Isabelle V. Kendig

Cooperating Units: National Institute of Neurological Diseases and Blindness

Man Years (calendar year 1957): Patient Days (calendar year 1957):

Total: .06 2
Professional: .01
Other: .05

Project Description:

Objectives: From the standpoint of the second investigator, the objectives in this study are to uncover developmental attitudes to the self and to the body image which may be related to the patient's present condition and perhaps enable a differentiation to be made between those suffering organic pain and those with psychological (phantom) pain.

Methods Employed: Data on early attitudes to the self and the body and family attitudes to illness are being obtained through the use of the Interview Schedule.

Patient Material: Patients included in the study of intractable pain being carried on by the principal investigator.

Major Findings: As only 4 persons to date have been seen in this study, there are no findings to report.

Significance of the program to Mental Health research: The problem of intractable pain is of great interest in medicine. If attitudinal factors are found to play an important role, particularly in connection with phantom pain, a new approach to treatment may be suggested.
Part A. Project Description Sheet (Cont'd.)

**Proposed Course of Project:** To carry it on until a sufficiently large group of patients has been seen to justify drawing conclusions re the psychological variables involved.

Part B included Yes [ ] No [X]
Part A.

Project Title: Drug Study

Principal Investigator: Conan Kornetsky

Other Investigators: Isabelle V. Kendig

Cooperating Units: Laboratory of Clinical Science, NIMH

Man Years (calendar year 1957): Professional: .2

Patient Days (calendar year 1957):
Total: .25
Professional: .2
Other: .05

Project Description:

See Serial No. M-CS-P-(C)-2

Part B included Yes [] No [X]
Project Title: Schizophrenic illness in a set of identical quadruplets

Principal Investigator: David Rosenthal

Other Investigators: Numerous NIMH investigators and personnel from other NIH institutes

Cooperating Units: None

Man Years (calendar year 1957): 2.6

Patient Days (calendar year 1957): 1460

Professional: .5

Other: 2.1

Objective: To determine factors related to the development of schizophrenia in a set of identical quadruplets and to evaluate factors which lead to differences in their psychopathology.

Methods employed: Interviews of the quadruplets, their relatives, and members of their home community. Observations of the quads and their parents. Biochemical, physiological, and psychological tests.

Patient Material: A set of 27 year old identical quadruplet girls.

Major Findings: A large amount of data of different kinds has been accumulated. The integration and evaluation of these data will begin on a more formal basis very shortly.

Significance of the program to Mental Health research: It is hoped that this intensive analysis will illuminate the process of schizophrenic development, especially with regard to genetic factors, social isolation, parental behavior, family life pattern, maturation of self-concept, and other related concepts.
Proposed Course of the Project: Data collection will terminate at the end of this year, and the formal integration and evaluation of findings will follow.

Part B included  Yes ☑  No ☒
Part A.

Project Title: Responsivity Patterns in Schizophrenics

Principal Investigator: David Rosenthal

Other Investigators: David Shakes, William G. Lawlor (visiting scientist), Theodore P. Zahn, Blanche Sweet

Cooperating Units: Clinical Sciences Laboratory (Ward 2-W) and St. Elizabeth's Hospital

Man Years (calendar year 1957): Patient Days (calendar year 1957):
Total: 2.15
Professional: 1.4
Other: .75

Project Description:

Objectives: Schizophrenics of various types are being studied with regard to how they respond at both the autonomic and molar behavioral levels when confronted by neutral, meaningful, and performance-demanding stimuli. The concepts of set and arousal are central in planning the program of studies, both with regard to the tests and procedures used and the measures taken. In the end, it is hoped to elucidate the responsivity patterns of various kinds of schizophrenics insofar as these may be influenced by externally induced psychological factors and by internal factors. With regard to internal factors, we hope in time to relate the phenomena here studied to studies of reticular activating and limbic systems in schizophrenics.

Methods Employed: Tests administered to date include: orienting (to light and tone; under amytal, amphetamine, and chlorpromazine); conditioning; reaction time; intelligence tests (WAIS and Progressive Matrices); Wisconsin Card Sorting Test, Rorschach; adaptation to blocking of alpha; discrimination of size differences; word-color test; and subjective probability tests. Eventually, when sampling will have become wider, tests will be intercorrelated to examine whether broad constellations of response patterns are present among schizophrenics.
Patient Material: One group of 13 schizophrenic patients having high, middle, and low percent time alpha in their electroencephalograms has been under study since July, 1957. A set of identical quadruplets with varying degrees of severity of schizophrenic symptomatology is also being studied. Till now, all patients have been Clinical Center patients, but plans have been in the making to include St. Elizabeths Hospital patients next year.

Major Findings: Data are now in process of being evaluated.

Significance of the program to Mental Health research: We hope to study the possibilities that:

1. Subgroups of schizophrenics can be differentiated according to their autonomic and molar behavior patterns.
2. These patterns can be related to schizophrenic symptomatology.
3. The subgroups can be differentiated according to genotypical background and/or family relationship constellations.
4. The pattern differences can be conceptualized as involving varying kinds of defect in "arousability".
5. Arousability defects are related to disturbances in the functioning of the reticular activating and/or limbic systems.

Proposed Course of the Project: We plan to evaluate the findings and to follow the best leads. Some tests and experiments may be modified and new ones will be planned on the basis of our initial findings.
Estimated Obligations for FY 1958

Total: $121,198

Direct: $89,956

Reimbursements: $31,242

Projects included: M-P-D(C) 1 through M-P-D(C) 17
Part A.

Project Title: The preparation of procedures for observing and recording infant behaviors and mother-child interactions in testing situations for use in a study of infant development. A pilot study.

Principal Investigator: Nancy Bayley

Other Investigators: Earl S. Schaefer

Cooperating Units: None

Man Years: Patient Days:
Total: .82 5
Professional: .40
Other: .42

Objectives: In preparing for a developmental study that is oriented toward finding significant variables in shaping personality structure, and rates of behavior development, it is necessary first to devise methods of observing, recording and evaluating the behavior of infants and their mothers during short testing-observation periods. The objective of this project is to devise and test a set of methods and recording procedures for such use.

Methods employed: Mothers and their young infants are visited in their homes where developmental and social tests are given the infants. At intervals each mother and child pair is brought into the Clinical Center for the same tests, at which time motion picture and tape recordings are made of the testing sequences. An earlier attempt to give these tests in a well-baby clinic proved unsatisfactory, and has now been dropped. A variety of methods of recording the procedures is being experimented with. Rating scales, adjective check lists, running accounts, coded records of responses made by observers during tests, and qualitative descriptive notes as well as the motion pictures are being tried out and checked for reliability, validity, and adequacy for purposes of interpretation.

Major Findings: This study is still in the stage of developing the tools of observation and recording, although several forms now being tried are promising. None of them is at present ready for general use.

Significance to the program of mental health research: Findings from other research indicate that the emotional health of infants and young children are affected by the emotional climate and characteristic
Significance to the program of mental health research continued: interaction patterns between children and significant adults. These emotional climates appear, furthermore, to affect significantly the course of behavior development. Much more information is needed on the ways in which these interactions occur, and on the extent of their effectiveness in determining mental health or disease. Careful observation in natural settings, with later evaluation of the same children is one of the best ways to discover the important variables.

Proposed Course of Project: Although this project was initiated as part of a projected developmental study of infants, the direction of interest of the members of the section is now shifted toward smaller, more intensive studies of infant behavior. Some of the forms developed here will be used in the mental test standardization. Others will be utilized as appropriate study conditions are instituted.
Part A.

Project Title: Standardization of the California Infant Scale of Mental Development

Principal Investigator: Nancy Bayley

Other Investigators: Marjorie P. Honzik and Dorothy H. Eichorn, University of California, Berkeley.

Cooperating Units: None

Man Years: Total: .55
            Professional: .25
            Other: .30

Patient Days: None

Project Description: Objectives: To revise and prepare for re-standardizing the California First Year Mental Scale to be extended through two years and re-named the California Mental Scale of Infant Development. The normative testing to be done by or under the immediate supervision of Drs. Marjorie P. Honzik and Dorothy H. Eichorn. The revision of the scale should fill a serious gap in the current status of developmental tests for infants. The infant scales now in use in this country were all standardized on data obtained 20 to 30 years ago on small samples of infants usually from a geographically, culturally and often socioeconomically restricted source. Because of these inadequacies of sampling, we have no assurance that the age norms in any of them are representative of infants in the country generally. The revision should be standardized by testing representative samples from a variety of geographical areas.

Aside from the sampling, however, current theories about the nature of the developmental processes call for inclusion in the scale of a wider range of behaviors in order to render the evaluations of a child's status more meaningful.

Methods employed: The original mental scale has been gone over item by item to make the procedural directions more clear; new items have been added for trial; new record forms and work sheets are being developed that will both increase the ease of administering and recording and allow for fuller descriptions of the infants' responses. An additional form has been devised for recording the child's emotional, attitudinal, energy output and goal-directed behaviors. These will be analyzed for age and developmental trends and for the relation of individual differences to scores of mental functioning.
Methods employed continued: Tentative revisions are tried out on a few infants and further revisions are then made. When satisfactory forms have been devised a program of testing will be instituted according to a statistical design that will insure good normative data.

Major findings: This project is now at the stage of selecting the items to be observed and developing the test form. A few infants have been tested for the purpose of discovering ways to improve the testing instrument.

Significance to the program of mental health: There is need for a really good objectively scorables well-standardized test of mental functioning in infants that covers the age span between birth and two years. This is of primary importance to basic research that is directed toward early detection of such conditions as mental deficiency and emotional disturbances. A good test would function as a basic tool in studies of environmental deprivation and the effects of emotional trauma on the infant's development and personality adjustment.

Proposed course of project: The testing procedures and record forms are now almost ready for putting into final form. The next step will be to organize the testing program. This is now in the preliminary planning stage.

It is probable that such a normative testing program will be tied into the large study of infant development that is being carried out in NINDB. In that program it is planned that 13-15 cooperating institutions will, over a period of eleven years, measure the development of some 35,000 children, starting with pregnancies, and continuing with the children until they are 5 years old. In this program well-standardized developmental tests are needed. It appears now that the processes of standardizing the two-year mental scale can be integrated with this program, in such a way that a standardization sub-sample can be derived from this total population. This in return would furnish standard test scores to the entire population, which would be tested less frequently.
Part A.

Project Title: Long-term experiences with methyltestosterone as a growth stimulant in short immature boys.

Principal Investigator: Nancy Bayley

Other Investigators: Gilbert S. Gordon and H. Lisser, University of California Medical School, San Francisco, California

Cooperating Units: None

Man Years: Total: .30
Professional: .15
Other: .15

Patient Days: None

Project Description: Objectives: To investigate the effects of oral administration of methyltestosterone on the growth and pubertal development of small immature boys.

Methods employed: Accumulated clinical records, including serial measurements of height, skeletal X-rays and treatment dosages of 100 boys, patients of Drs. Lisser and Gordon, were studied. Growth curves of height, and annual increments were plotted on Bayley's curves. Skeletal ages were read from the X-rays and pre-treatment height-predictions made on 62 of the boys, using the Bayley-Pinneau tables. Subsequent height predictions, after treatment were possible from later X-rays of 36 of the boys. It was possible to compare the predictions with eventual adult stature for 20 boys whose growth was completed. The effect of methyltestosterone on growth were found to be most effectively evaluated by grouping the boys according to age at maximum growth.

Major findings: Small doses (5 to 20 mg.) of methyltestosterone were found to result in immediate spurts of rapid growth in most instances. Compared with pre-treatment predictions, both post-treatment predictions and actual adult statures were found to be, with few exceptions, at or above the expected growth without treatment. Few disturbing side-effects were noted.

Significance to the program of mental health research: Small boys, who are retarded in puberal development, have been found to have emotional problems related to their small size, lack of strength, and immaturity. If growth can be stimulated at the normal age for such growth without physical damage, these boys may be helped to regain status and thus reduce their emotional problems.

Proposed course of project: Completed and published.

Part B included Yes / / No / /
tB: Publications

Publications other than abstracts from this project:

Part A.

Project Title:  Relationship of maternal behavior to the subsequent social, emotional, and intellectual development of children.

Principal Investigators:  Nancy Bayley and Earl S. Schaefer

Other Investigators:  None

Cooperating Units:  None

Man Years:  Professional: .40

Other: .42

Patient Days:  None

Project Description:  Objectives: Recent theories of the effects of maternal behavior upon personality development of children have shifted from an emphasis upon such variables as age of weaning and toilet training to variables which stress social and emotional behaviors of the mother with the child. In another project data collected by Bayley in the Berkeley Growth Study have been utilized in developing a method for quantifying notes on behavior observation of mother-child interactions of children under 3 years and of unstructured interviews of the mothers when the children were approximately 10 years old. The objective of this project is to study the relationship between these maternal behavior variables and the intellectual, social, and emotional behavior data on children which were collected by Nancy Bayley over a period of twenty-one years. Some of the analyses will test current theories of the influence of the mother upon the development of the child while other analyses will explore the data in an effort to develop new hypotheses which can be tested in future studies.

Methods employed: Much of the data on the children was recorded in quantified form, e.g., intelligence scores, ratings of behavior in the test situation at various ages, tests of interests and attitudes, and many others which were collected over a period of 21 years. Other records on the children consist of unstructured notes on test behavior, notes on interviews, projective test materials, etc. One phase of the project is to develop a method of quantifying personality concepts from the available data. A rating scale is being developed to quantify notes on test behavior between the child's age of 11 to 18. It is often necessary to group other scores. Appropriate statistical techniques to analyze reliability consistency through time, and the relationships of the various variables with one another and with maternal behavior must be selected and statistical
Part A. continued:

Methods employed continued: analyses of the material must be done. The data are being organized to permit the application of IBM techniques in order to facilitate the analysis of this comprehensive and unique set of longitudinal data.

Major Findings: All results of these data indicate differences between the relation of maternal behavior to personality development of boys and personality development of girls. Maternal behavior is consistently more highly related to intellectual and personality development of boys than girls. This finding may be relevant to the process of identification in males and females. Another finding is that upper socioeconomic groups tend to show more positive behavior toward their children. This may help in interpreting differences in incidence of mental health problems among socioeconomic groups. Maternal behavior is significantly related to the intellectual development of males but not of females. Mothers who are Cooperative, Equalitarian, and Express Affection for their children most often have sons who consistently improve in intelligence through the first 6 or 8 years, and then remain stable, while the opposite is true for mothers who are Punitive, Irritable and Ignoring. Maternal behaviors which are approved by mental health specialists are related to the happiness, calmness, and positive behavior of their children between 10 months and three years of age. It was found that behavior ratings of children of this age level largely define two dimensions—Happiness vs. Unhappiness and Activity vs. Passivity. The child's activity between 10 months and three years is more consistent than the child's happiness, though neither characteristic is highly consistent.

Maternal behavior variables are significantly related to the rated behavior of boys in the test situation between three and nine years of age. The pattern of relationship of maternal behavior with the rated behavior of girls is less clear. Maternal behavior is also significantly related to the test behavior of boys between 11 years and 18 years. Analysis of these data on the girls is incomplete. Reliable ratings of adolescent behavior in the test situation were obtained from the rating scale which was developed.

Correlations among the maternal behavior variables which are reported in another project revealed two primary dimensions of Love vs. Hostility and Autonomy for the Child vs. Control. An investigation of the consistency of maternal characteristics between the two age levels revealed relatively high consistency of the Love vs. Hostility dimension but low consistency of the Autonomy vs. Control dimension. This result was meaningful in that the child's needs for autonomy vary from total dependence at birth to relatively complete independence as an adult while his needs for positive relationships are relatively consistent through time. The detailed information on intelligence and personality which is available on this group over a
Part A continued:

**Major Findings continued:** Period of 21 years has resulted in other findings which are relevant to hypotheses of the influence of environmental variables upon development. Intensive study of these results and their interpretation is necessary before their significance can be determined.

**Significance to the program of mental health research:** Since most of the theories of family influence upon personality development have been developed from clinical and retrospective studies, the opportunity to test them developmentally should assist materially in evaluating these theories. The data on social and emotional interactions of mothers with their children from both observations and interviews are unique since most data on maternal behavior are from structured interviews with no opportunity to check their validity. The results of this study are highly relevant to the theories of Sullivan, Fromm, and Horney which are currently influential among psychiatrists and psychologists and should be valuable in testing those theories. Data about personality and intellectual development which are valuable to personality theory and to the mental health movement may be obtained.

**Proposed course of project:** Further investigations on the interrelationships of these data will be made. The data will be prepared for IBM analysis and the results will be interpreted and reported.

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Part B included Yes [ ] No [X]
Project Title: Development of a theory of the role of parental behaviors in the etiology of personality structure and psychopathology.

Principal Investigator: Earl S. Schaefer

Other Investigators: None

Cooperating Units: None

Man Years: 
Total: .37
Professional: .20
Other: .17

Patient Days: None

Project Description: Objectives: The purpose this research is to develop a systematic theory of the effects of social influences upon personality development and to develop a theory of the relationship of the major diagnostic categories to one another and to the healthy personality. As systematic theory would enable one to integrate personality research, both clinical and experimental, into a common conceptual scheme in which the various findings would be relevant to one another. A theory would guide future research designs as well as assisting in interpreting previous results.

Methods Employed: Through an important advance in statistical theory, Guttman's circumplex theory, a new way of investigating the inter-relationship of personality variables became available. The circumplex method, which is a search for a law of neighboring and a law of polar opposites in a set of correlations, permitted a parsimonious ordering of a set of maternal behavior concepts which had been developed by Schaefer, Bell, and Bayley in a previous project in this laboratory. This parsimonious ordering of maternal behavior concepts was found to apply to other published data and to other concepts which have been used to describe maternal behavior. Hypotheses were developed concerning the types of personality structures which might be developed from the accumulative effective of the different maternal behaviors. Predictions were made and the predictions were verified from empirical data. Proposed work on the theory is to apply the theory as it exists to further published data, to amplify or modify the theory as indicated by these data, and to plan additional studies which would test the theory.
Major Findings: Two major dimensions of maternal behavior have been isolated--Love vs. Hostility and Autonomy for the Child vs. Control. A prediction was made that Love and Autonomy would result in a normal personality adjustment, Love and Control in a more inhibited neurotic personality, Hostility and Control in a more schizoid personality, and Hostility and Autonomy in a more psychopathic, delinquent personality. This prediction specified the relationship between the various diagnostic types and the normal personality. The prediction was substantially verified by intercorrelations of the scales of the Minnesota Multiphasic Personality Inventory which were developed to differentiate the diagnostic categories. Additional verification was found in published data from the comprehensive assessment data of the Institute of Personality Assessment Research and in several comprehensive behavior rating studies on Nursery school children, pre-adolescents, and young adults. The findings were related to Freudian theory, to data on psychotherapeutic success, to learning theory, and to the literature on experimental neurosis in animals.

Significance to the program of mental health research: Current psychiatric theories of Sullivan, Fromm and Horney stress the effect of environmental factors upon personality development. The development of a systematic theory of the nature of these social environmental factors and of their effect upon personality development will organize, amplify, and clarify these theories. This theory will permit the integration of available data and the development of improved research designs for future studies of the effects of the social environment upon personality development. The conceptual scheme also simplifies the problem of communication mental health concepts since it organizes an extremely complex phenomenological field into an ordered and parsimonious set of concepts.

Proposed course of project: A paper entitled "A theory of personality development, personality structure, and psychopathology" is in preparation and will be sent to Behavioral Science. Further data will be obtained from published studies and further tests of the theory will be made in new research designs.
Part A.

Project Title: Organization of Maternal Behavior and Attitudes Within a Two Dimensional Space.

Principal Investigator: Earl S. Schaefer

Other Investigators: None

Cooperating Units: None

Man Years: Total: .37 Professional: .20 Other: .17

Project Description: Objectives: One of the major goals of science is to order an apparently complex phenomenological field into a parsimonious, ordered set of concepts. Previous researches in this laboratory by Schaefer, Bell, and Bayley have developed a Parental Attitude Research Instrument and a Maternal Behavior Research Instrument with which to conceptualize and quantify parental attitudes and behaviors. Papers on these research instruments are now ready for publication. The purpose of this research is to study the interrelationships of the concepts which are measured by these research instruments in order to be able to develop efficient research designs, to assist in interpreting research results, and in order to be able to develop a comprehensive theory of the effects of maternal behavior upon the personality adjustment of children.

Methods Employed: Quantified data on maternal attitudes and behavior were intercorrelated, and the methods of factor analysis and Guttman's radex analysis were used to discover a simple nomological network within the concepts.

Major Findings: Both methods revealed two major dimensions of both maternal attitudes and behavior which were labelled Love vs. Hostility and Autonomy vs. Control. These two dimensions included most of the common factor variance of maternal behavior with the child. The discovery of this order among the maternal behavior concepts was generalized when it was found that other published data on maternal behavior could also be organized by this two dimensional scheme.

Significance to the program of mental health research: Recent studies of personality development in psychiatry, sociology, and psychology have emphasized the great importance of the family and of the mother.
Part A. continued:

Significance to the program of mental health research continued:
Although there is some concensus about the important variables, due to
different terminologies and to the apparent complexity of the data, no
organized conceptual scheme which could integrate this research has
been available. It appears this two dimensional organization of
maternal behavior which we are developing would make it possible to
integrate many of these researches.

Proposed Course of Project: Papers on this organization of maternal
behavior and attitudes are being prepared. Further confirmation and
amplification of the conceptual scheme will be attempted in conjunction
with other projects and from other published data.

Part B included Yes [ ] No [XX]
Part A.

Project Title: Development of a Maternal Behavior Research Instrument.

Principal Investigators: Earl S. Schaefer, Richard Q. Bell and Nancy Bayley.

Other Investigators: None

Cooperating Units: None

Man Years: Total: .67  Professional: .40  Other: .27

Patient Days: None

Project Description: Objectives: The purpose of this research was to develop a conceptual scheme and a method of quantifying maternal behavior both from behavior observations and interviews. In order to be able to test theories of the effects of maternal behavior upon personality development of children it was necessary to organize two sets of data that had been collected by Dr. Bayley at the Institute of Child Welfare at Berkeley.

Methods Employed: The set of concepts which had been developed by Schaefer and Bell in the project which developed the Parental Attitude Research Instrument were revised and attitudinal concepts were added. Several trait-actions or specific behaviors were specified which defined each of the abstract concepts. Each of the trait-actions were rated on a seven point scale by each of the three judges for each case. By combining the several trait actions which defined each abstract concept and by combining the ratings of the three judges reliable scores on the maternal behavior concepts were obtained. This method was applied to sets of ten to twenty observations on each of 56 mothers on whom notes had been written from the child's age of one month to three years and to 34 sets of one to two interviews with the mothers at the child's age of approximately ten years.

Major Findings: The method resulted in reliable ratings of maternal behavior from both behavior observations and from interviews. It was possible to define the abstract general concepts with specific behaviors of mothers and to get agreement between judges from unstructured written behavior observations and interviews which had not been collected with this conceptual scheme in mind.
Part A. continued:

Significance to the program of mental health research: Clinical reports have emphasized the contribution of the mother to the personality development of the child yet few attempts have been made exactly to define or to quantify the concepts used. Many longitudinal studies of personality development have collected unstructured observations and interviews with mothers but no method has been available with which to quantify these data in terms of social-interaction concepts. The development of this rating scale will permit quantification of unstructured observations, interviews and clinical descriptions of mother-child interaction and will assist in testing theories of maternal influence upon personality development.

Proposed Course of Project: A paper on this project has been prepared and is being submitted to Child Development. The method will be used in future research. Project completed.
Part A.

Project Title: Origins of Emotional Dependency in Early Childhood: An Experimental Program.

Principal Investigator: Jacob L. Gewirtz

Other Investigators: None

Cooperating Units: None

Man Years:                           Patient Days
        Total:      1.07                         None
        Professional:       .45
        Other:           .62

Project Description: Objectives: To inaugurate a program of research in infants and young children on the basic acquisition processes underlying 'emotional dependence'. It is intended to focus particularly upon children's behaviors like those employed to gain such positive social responses from adults as their attention, affection, approval, nearness, and caresses, and upon the earliest environmental conditions under which they develop.

Methods employed: Proceeding both from simple learning and performance concepts and from such theories as are available for tracing the early development of emotional dependence, it is intended to analyze the apparent complexities of that behavior class into skeletal terms, so that they may be related in a simple manner to the fundamental mechanisms operating in the developing child.

Methods are being explored with very young children which reduce to relatively simple terms the complexities of the behavior which characterize emotional dependence in later childhood and which would relate those behaviors to critical aspects of myriad environmental conditions to which young children are typically subject. A series of prototype experiments with human infants in a highly controlled institutional setting represents the core of the experimental program. Initially, these experiments will attempt to relate effects in the child's pattern of emotional dependence to variations in selected aspects of the caretaking process, analyzed in terms of learning contingencies. At first, the reinforcing aspects of caretaking and adult responsiveness to the child are employed as variables; and the range of adult responses which can function as reinforcers for the young child's behavior will be explored. Selected stimulus events associated with the caretaker are being set into a variety of contingencies with different responses emitted by the child. In addition, the attempt will be made
Methods employed continued: to determine if environmental change or novel stimuli as, for example, noises or lights, within and without the caretaking process, can function to reinforce the child's behavior.

After some of the more common reinforcers which are provided by adult responses are determined, selected stimulus events (e.g., the attention of a caretaker) involved in or attached to the caretaking person may be set into a variety of contingencies with these reinforcing aspects of the caretaking process; and selected aspects of this process may be made contingent upon different responses emitted by the child.

Major findings: While this project is in its initial phase, some recent research (with Dr. H. Rheingold) suggests that a vocal response in three-month old infants can be conditioned through use of an adult's complex social response as reinforcing stimulus.

Significance to the program of mental health research: While it is probable that an understanding of the processes underlying emotional dependence will be critical to the understanding of a substantial portion of the social behavior both of children and adults, potentially useful to the theory of child rearing as well as to therapeutics, almost nothing is known either about the dimensionality or the antecedents of that behavior class. This research program constitutes a beginning in the direction of gathering such information under highly controlled conditions.

Proposed course of project: The "tooling-up" phase of the research program may require another six months before it will be fully underway. At that time equipment should be available to study a single infant at any one time. The project will require a population of infants, and the search for such a source is now going on. Suitable experimental techniques are now being devised.

Part B. included: Yes [✓] No [✗]
Part A.

Project Title: The Effects of Deprivation and Satiation on Social Reinforcers

Principal Investigator: Jacob L. Gewirtz

Other Investigators: None

Cooperating Units: None

Man Years: 
- Total: 1.11
- Professional: .49
- Other: .62

Project Description: Objectives: Events which are the "goals" of human social behavior are termed "social reinforcers." More specifically, a social reinforcer is defined as a social stimulus event which, if made contingent upon behavior, can systematically affect its output. It is generally assumed that social reinforcers (e.g., attention, approval, affection) have developed importance for people through a history of conditioning.

Deprivation implies a period of unavailability of a given reinforcer which results in an increase in behaviors for it; satiation implies a period of availability of a reinforcer sufficient to effect a decrease in behaviors for it. Thus deprivation and satiation represent two statements of a single concept, a dimension characterized by the relative supply of a given reinforcer in the recent history of the organism which determines the incidence of behaviors for that reinforcer. Laws relating long-and short-term social deprivation as an empirically defined dimension to certain basic characteristics of social behaviors would have considerable integrative value (d.f., e.g., Spitz, Bowlby, and others). But first the experimental operations of deprivation and its inverse, satiation, must be implemented in social terms.

Social reinforcers may be supplied and deprived in a variety of ways, and it is important to discover their responsiveness to many of these ways. It would be especially important, for example, to implement the deprivation of a single social reinforcer, rather than of all such reinforcers (as, for example, is accomplished through social isolation in these studies). Further, it is essential to have some assurance that social reinforcers are more or less homogeneous in this regard.
Methods employed and Major Findings to date: (1) Brief social isolation (equated to a condition of deprivation of all social reinforcers) increased reliably the reinforcing power (i.e., the importance) of adult approval for children (aged 4-0 to 5-6) as a positive function of the degree to which they typically sought such approval in other settings; and older children in this age range were affected to a greater extent than were younger children. (2) In children aged 6-6 to 9-0, it was found that brief social isolation (deprivation) enhanced the effectiveness of social reinforcers representing approval and social contact relative to a control condition (no treatment); and that a brief condition of satiation for approval and social contact decreased the effectiveness of those social reinforcers relative to the control condition.

Significance to the program of mental health research: This project is a beginning attempt to gain an understanding of some classes of short- and long-term conditions constituting social deprivation, a concept of importance particularly in the child health literature. At the same time it would provide additional understanding of the social reinforcers (social goals) important for children, and possibly an understanding as well of the conditions under which they develop.

Proposed Course of Project: This is a program of research: a number of studies are being published, and as additional studies are completed, new ones will be begun. As relevant variables are isolated, it is intended that they be investigated parametrically where possible.
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:

The effects of deprivation and satiation on behaviors for social reinforcers. (with D. M. Baer) *American Psychologist, 1957, 12, 401.*

The effect of brief social deprivation on behaviors for a social reinforcer. (With D. M. Baer) *Journal of Abnormal and Social Psychology,* in press.

A note on the similar effects of low social availability and deprivation on young children's behavior. (With Baer and Roth) *Child Development,* in press.
Part A.

Project Title: A screening test for selecting parents on the basis of their attitudes toward children: relations between attitudes expressed during the lying-in period and later behavior with the one-month old infant.

Principal Investigator: Richard Q. Bell

Other Investigators: Belinda Straight (Guest Investigator)

Cooperating Units: None

Man Years:
- Total: 1.21
- Professional: .57
- Other: .64

Patient Days: 34

Project Description: Objectives: To test the hypothesis that attitudes toward child rearing practices expressed by mothers during the lying-in period are related to behavior with their infants at a later point in time.

Methods Employed: Primiparous mothers are assigned to a sub-group having a characteristic attitude pattern on the basis of responses to a self-reporting attitude questionnaire administered during the lying-in period. The existence of such sub-groups was established by statistical procedures carried out in project NIMH 114(C) 1955. The mother's behavior with her infant at the time of a one-month follow-up is rated on a variety of scales developed in project NIMH 116(C) 1955. Similarity of mothers on the basis of such scales should be greater within sub-groups than between sub-groups if the parental attitude questionnaire is related to actual interaction with infants in any comprehensive way involving a variety of behavior. It is not necessary that there be direct correspondence between what the mother says on the attitude questionnaire and how she behaves with the infant.

Major Findings: The data gathering stage has been completed, but data analysis will require a major portion of the coming year. It is the impression of the investigators that the one-month follow-up examination used in this study provides relatively rich data on the nature of the mother-infant relationship. It was possible to identify five mother-infant relationships which seemed incipiently pathological. This suggested to the investigators that a future study might be designed specifically to test the adequacy of a first and second line mass screening approach, an initial screening during the lying-in period,
Part A. continued.

Major Findings continued: followed by a more intensive screening in the follow-up examination at one month. This type of study would require sampling a much more extensive population than the study currently underway which sampled only from specified statistical sub-groups.

Significance to the program of mental health research: If psychologically useful sub-groups can be identified it will simplify statistical operations involved in screening any population of young parents for those likely to form pathological relationships with their children. A one month follow-examination could be used as a second-line of screening to reduce the margin of error in the initial screening. The present study is an initial attempt to test out such screening operations on a limited scale with selected sub-groups from a larger population.

Proposed Course of Project: Calendar year 1958 will be spent in analyzing data now collected, and if useful results emerge sufficiently early it should be possible to resume screening and follow-up procedures to focus on any leads which emerge.

Part B included Yes [ ] No [ X ]
Part A.

Project Title: Early Infant Personality Characteristics: Studies of orality, activity, and sensitivity in neonates.

Principal Investigator: Richard Q. Bell

Other Investigators: None

Cooperating Units: None

Man Years:
- Total: .97
- Professional: .33
- Other: .64

Patient Days: None

Project Description: Objectives: The objective of this project is to obtain some precise measures of infant characteristics in the immediate post-natal period. These characteristics will be used to test the hypothesis that infant types exist prior to exposure to maternal care.

Methods Employed: Motion picture records have been made of 31 infants 96 hours old from which estimates are being made of cutaneous and kinesiologic sensitivity, auditory sensitivity, visual sensitivity, depth and amount of sleep, strength and muscle tone, reaction to frustration, feeding characteristics, nature of crying, and appearance. Measurements of feeding characteristics are based on an apparatus which when filmed in use reveals rate, rhythm, and vacuum created in sucking. Other variables are estimated by rating infant behavior directly. Precision is achieved by repeated viewing of the films and making direct comparisons between babies. Film records have also made it possible to detect and evaluate the effects of any deviation from standard circumstances or test administration at the time observations are being made.

Major Findings: Although reliable rating of infants at this age has been difficult to achieve in other studies, use of the film technique has made it possible so far to achieve reliable measures of five of the variables rated up to date. No findings will be available until the remaining ratings are completed.

Significance to the program of mental health research: Research on the effects of parent behavior on the emotional adjustment of children is handicapped by the fact that different children provoke different behavior from their parents as well as react differently to their parents. Attempts by other studies to identify congenital patterns in infants have led to confusing results since very little consistency on individual measures has emerged over time. The present study will attempt to identify congenital infant types, and test the notion that infants will
Significance to the program of mental health research continued: at later points in time fall into the same generic types even though the basis of their being grouped has changed due to metamorphic growth processes. Thus consistency of pattern may be demonstrable in spite of lack of consistency in individual measures correlated over different time periods.

Proposed course of project: The ratings should be completed during this calendar year and some information on whether clusters or types exist should be ascertainable soon thereafter. During calendar year 1958 these data will be related to observations made on the same infants at one month. This project serves an independent purpose in studying congenital patterns in infants as well as providing control data for a related study NIMH--P-3(C) which compares mother-infant interaction in mothers grouped into one of five groups based on an attitude questionnaire. This project provides data on whether the infants born to the mothers in the five groups differ significantly prior to leaving the maternity hospital.
Part A.

Project Title: Further Studies of the Conditioning of Vocal Behavior in the Human Infant.

Principal Investigator: Harriet L. Rheingold

Other Investigators: None

Cooperating Units: None

Man Years (calendar year 1957): 0.05

Professional: 0.05

Other:

Project Description:

Objectives: The results of the first study suggest that the social vocalizations of three-month-old infants were conditioned (i.e. increased) by means of a social reinforcer. Several questions were raised and require further study before the results can be unequivocally attributed to the experimental procedures. The first of these asks to what extent the stimulating properties of the reinforcer might have been responsible for the increase rather than its having been made contingent upon the child's vocalizing. The second asks whether home babies would respond similarly to the original institutional subjects. The third asks questions about the effect of different schedules and their use over longer periods of time.

Methods Employed: Both home and institutional babies will be used. Intensive studies will be made of a few children, now that a result has been demonstrated in large groups of infants. To test the stimulating properties of the reinforcer, the reinforcer will be administered at regular intervals (e.g. 10" apart) but never directly after a vocalization. To further test the possibility that operant conditioning did occur in the original experiment, some work should be done with different
Part A. Project Description Sheet (cont'd.)

schedules, with both fixed and variable ratios, with reconditioning after extinction, with continuing conditioning until certain predetermined rates of vocalizing are obtained.

**Major Findings:** These studies are in the planning stage.

**Significance of the program to Mental Health research:** If conditioning of any behavior can be obtained in the three-month-old human infant, we have learned an important fact about human learning. If, further, social behavior proves to be modifiable by environmental response, specifically a social response, we are closer to accounting for early differences in sociability. Finally, since the social behavior here studied is vocal, we may obtain clues to the later use of speech for social and perhaps other purposes.

**Proposed course of the project:** The study will be begun in the next month or two.

Part B included  Yes [ ] No [X]
Part A.

Project Title: The Chick's Preference for Some Visual Properties of Water.

Principal Investigator: Harriet L. Rheingold

Other Investigators: Dr. Eckhard H. Hess, Department of Psychology, University of Chicago.

Cooperating Units: None

Man Years: Patient Days:
Total: .20 None
Professional: .10
Other: .10

Project Description: Objectives: The chick discovers and drinks water very soon after hatching. On the assumption that water must possess some characteristic or pattern of characteristics which draws the chick to it, we set out to analyze the "attractiveness" of water's visual properties. The questions asked were: What are the visual properties of water which attract the naive chick? To what extent are these changed as the chick acquires experience with water?

Methods Employed: Newly-hatched chicks were presented with an array of six stimuli, namely water and five other substances, each of which possessed some, but not all, of the visual attributes of water. The subjects were 100 White Rock chicks. Seventy-two of these, having no experience with food or water, were tested at the age of three days. Twenty-eight were control chicks also tested at the age of three days, but these had been given food and water from the time of hatching. All animals were tested again four days later, both experimental and control animals having had access to food and water in the interval, except for 12 hours of water deprivation just prior to the tests.

Major Findings: The distributions of responses given by experimental and control animals at both ages were similar. The order of stimuli for chicks three days old was mercury, plastic, blue water, water, metal, and red water. Experience with water did not alter the
Part A. Project Description (cont'd.)

position of mercury as first "choice" and of water as fourth. It seems probable that attractiveness to the chick lies in a combination of a bright reflecting surface and the movement of the stimulus.

Significance to Mental Health Research: Some investigators believe that behavior may be released by stimuli which are prepotent for the species, i.e., that certain stimuli are "innately releasing." While this principle may be truer for lower-order species, it may also account for some of the behavior of other species, e.g. the human infant. The present study demonstrates a method by which this principle can be tested.

Proposed Course of Project: This study was executed in 1955 at the University of Chicago. It was prepared for publication at NIH in 1956, and in 1957 it was accepted for publication by the Journal of Comparative and Physiological Psychology.

Part B included    Yes [X]    No [X]
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:

Rheingold, Harriet and Hess, Eckhard. The Chick's Preference for Some Visual Properties of Water. Accepted for publication by the Journal of Comparative and Physiological Psychology.
Part A.

Project Title: Increasing Social Vocalizations in the Infant by Means of an Adult's Social Response (formerly: The effect of social reinforcement upon social behavior in the human infant: the effects upon vocal behavior.)

Principal Investigator: Harriet L. Rheingold

Other Investigators: Jacob L. Gewirtz

Cooperating Units: None

Man Years: Patient Days:
Total: .90 2
Professional: .40
Other: .50

Project Description: Objectives: Vocalizations are a prominent component of the response three-month-old infants give to an adult. In turn, adults often respond to these vocalizations. If the adult's responses are made contingent upon the infant's vocalizing, thus functioning as a social reinforcer, will the infant increase his rate of vocalizing?

Methods Employed: Twenty-two three-month-old infants were studied in two separate experiments. In one experiment 11 babies were reinforced by one experimenter; in the other, 11 different babies were reinforced by another experimenter. The basic unit of measure was the number of discrete vocalizations produced by an infant during three-minute periods. Vocalizations were counted for nine three-minute periods distributed throughout a day.

In the baseline condition, the first two days, E leaned over the baby and looked at him with an expressionless face. Under conditioning, the next two days, E reinforced vocalizations by simultaneously smiling clucking, and lightly pressing the infant's abdomen. During the last two days, extinction, E returned to the expressionless face of the baseline condition, and made no response to the infant's vocalizations.

Major Findings: By means of the social reinforcer the number of vocalizations was raised from the baseline mean of 13 to a mean of 24.8, an increase of 86.5%. Removing the reinforcer depressed
Part A. Project Description (cont'd.)

The rate until by the second day of extinction it was close to the level of baseline performance. The results suggest that (a) verbal behavior produced by three-month-old babies in a social situation can be very quickly brought under control and (b) an everyday complex of acts, typical of a mother's social behavior can function as a reinforcer.

Significance for Mental Health Research: This is part of a larger inquiry into how different components of mothering influence the development of social behavior in the human infant.

Proposed Course of Study: The study has been completed and the data analyzed. It was reported at the 1957 American Psychological Association meetings and now is being prepared for publication.

Part B included Yes □ No □
Project Title: A Follow-Up Study of Social Responsiveness in a Group of Institutional Babies.

Principal Investigator: Harriet L. Rheingold

Other Investigators: Nancy Bayley

Cooperating Units: None

Man Years:
- Total: .46
- Professional: .20
- Other: .26

Patient Days: None

Project Description: Objectives: Eight experimental infants, as a result of special mothering, showed a marked increase in social responsiveness with little, if any, significant increase in intellectual performance. One year after termination of treatment both experimental and control babies were tested to discover if the experimental babies showed any persisting effects of treatment.

Methods Employed: Fifteen children were located and examined in their own homes by the second investigator who did not know the children's experimental status. All but one of the children had left the institution for their own or adoptive homes. They were given the Cattell Infant Intelligence Scale and a specially constructed test of social responsiveness. Incidental information was obtained on the mother and the home.

Major Findings: The babies were found to be living in a great variety of different life situations. The "intellectual" performance of both groups was practically identical. The experimental subjects, however, were more responsive (when positive and "negative" reactions were given equal weights) than the control subjects (p at the .1 level). Especially interesting were the marked negative responses shown by two experimental subjects.

Significance for Mental Health Research: Generally it is assumed early experience will affect later behavior. This study seeks to
Part A. Project Description (cont'd.)

discover the extent to which this assumption may be accepted in the case where social behavior was modified in the sixth, seventh, and eighth months of life and then assessed one year later.

Proposed Course of Project: The data have been analyzed. The study will be written up for publication.

Part B included Yes ☐ No ☒
Part A.

Project Title: The Differential Responsiveness of Infants to Familiar and Unfamiliar Persons.

Principal Investigator: Harriet L. Rheingold

Other Investigators: None

Cooperating Units: None

Man Years: Patient Days:
Total: .38 None
Professional: .15
Other: .23

Project Description: Objectives: It was predicted that infants responsive to the social overtures of a person with whom they were familiar, even though this person had performed few, if any, caretaking acts for them, than they would be to a person totally strange.

Methods Employed: In order to test the proposition the responses of 40 institutionalized infants, 4 to 10 months of age, were obtained to three different persons. The first was the person in charge of the floor who had some contact with all the babies but who did not routinely perform caretaking services for them. The second was an unfamiliar person who wore the same distinctive garb as the first person. The third person had never been seen by any of the babies before the day of testing. In garb she did not resemble the first person but instead the class of persons who regularly cared for the babies. The order in which the three persons presented themselves to the babies was systematically varied.

Major Findings: The infants appeared to be most responsive to the third person, the stranger. Two possible explanations are being explored. One is that the stranger possessed greatest novelty value. The second is that the response to the stranger represents a response which has generalized from the infants' experiences with caretakers who, in general, were constantly
Part A. Project Description (cont'd.)

changing persons (volunteers).

A more detailed analysis is now in process. Contemplated are
studies of the contribution each subtest makes to the total score;
of the extent to which subtest scores cast light upon the mechan-
isms responsible for the differences in response to the three
persons; of the ratio of positive to "negative" responses accorded
each person; of number of vocalizations made by the infant in re-
sponse to each person; of changes in response with age. Responses
can be compared with those given a constant caretaker (obtained from
an earlier study).

Significance for Mental Health Research: This study is part of a
larger program which seeks to explore the development of socia-

bility in the infant. It is assumed that early manifestations of
social behavior influence later behavior and that social behavior
is central to an understanding of personality.

Proposed Course of Project: The data have been gathered and are
being analyzed.

Part B included   Yes [ ]   No [ X ]
Project Title: The Effect of a Strange Environment upon the Behavior of Infants.

Principal Investigator: Harriet L. Rheingold

Other Investigators: None

Cooperating Units: None

Man Years:_patient_days:
Total: .55
Professional: .30
Other: .25

Project Description: Objectives: It is predicted that infants, even in the first few months of life, are sensitive to changes in both the physical and human components of their environment. This study seeks to discover the kinds of behavior which are affected by change, the degree to which they are affected by situations ranging from minimal to maximal change, individual differences in reactions and the relationships between these variables and the infant's age.

Methods Employed: Several related studies are planned, using home and institutional babies, in situations which involve different kinds and amounts of change. The first pilot study is being carried out on twins, who are examined at monthly intervals both in their home and in the Clinical Center, usually on successive days, the order of place of examination being alternated regularly.

Major Findings: By the fifth month of age the babies began to give a more restricted performance at the Clinical Center on the tests used, that is, on tests of social responsiveness to the mother and to a stranger, and on tests of developmental progress. At present the twins are eight months of age.

Significance for Mental Health Research: The general problem is the charting of the growing awareness of, and sensitivity to, the environment in the human infant. The problem can be attacked by measuring his responses to changes in his environment. The term
Part A. Project Description (cont'd.)

"environment" is conceived broadly and includes both people and things. Some changes may produce an acceleration of growth, some may inhibit it. In another sense, change may be viewed as frustrating, and the alternations in behavior as modes of defense.

Proposed Course of Project: The twins will be examined monthly until they are twelve months old. After the results are analyzed, a more definitive study will be set up.

Part B included Yes ☐ No ☒
Estimated Obligations for FY 1958

Total: $92,675

Direct: $69,597

Reimbursements: $23,078

Projects included: M-P-P(C) 1 through M-P-P(C) 12
Part A.

Project Title: Communication of Value Systems Between Therapist and Schizophrenic Patients

Principal Investigator: Morris B. Parloff, Ph.D.

Other Investigators: Norman Goldstein, M.D., Boris Iflund, Ph.D.

Cooperating Units: None

Man Years (calendar year 1957): Patient Days (calendar year 1957):
Total: 68 None
Professional: 20
Other: 48

Project Description:

Objectives: To devise techniques for the study of the process by which the schizophrenic patient learns the therapist's value system regarding therapy, and by which the therapist learns the patient's values.

Methods Employed: Topics introduced by schizophrenic patients in daily psychotherapy sessions were recorded by observers and presented to the patient and therapist at the end of each session. Topics were independently rank ordered by therapist and patient regarding importance for therapy. Each participant also predicted the sortings of the other. Changes in understanding and convergence of values over time was compared for improved and unimproved patient.

Patient Material: The study focusses on two paranoid schizophrenic cases treated individually by the same therapist over a period of approximately two years. One patient recovered.

Major Findings:
1. The therapist's values regarding the importance of content for psychotherapy is communicated to the patient.

2. Acceptance by the patient of the therapist's values varies consistently with such factors as day of the week and therapist's responses and activity level.
Part A. Project Description (Cont'd)

3. A positive relationship was found between the therapist's mode of response to a topic ("approving" or "disapproving") and the rate at which the patient subsequently introduced the topic.

4. Although the patient's choice of topics appeared to be consistent with the therapist's expressed values, the patient's own evaluation of these topics in some instances, moved quite independently.

5. A patient's verbal behavior may appear to be superficially compliant to the unconsciously expressed expectations of the therapist, without the patient having internalized such therapist-values.

Significance to the Program of Mental Health Research: Basic to the understanding of psychotherapeutic treatment of schizophrenia is the understanding of the interrelationships between therapist and patient. It is this relationship that provides the conditions which permit the patient to learn that it is safe to give up his defenses and to learn more adaptive ways of relating. The above technique permits the study of the factors influencing the learning process which occurs in therapy.

Part B included - No
Part A.

Project Title: Nature and Stability of Psychiatric Nurses Concepts of Their Roles

Principal Investigator: Morris B. Parloff, Ph.D.

Other Investigators: Charlotte Schwartz, M.A., Wm. C. Jenkins, M.D.

Cooperating Units: Adult Psychiatry Branch, Socio-Environmental Studies, and Laboratory of Clinical Sciences

Man Years (calendar year 1957): 88
Professional: 20
Other: 68

Patient Days (calendar year 1957): None

Project Description:

Objectives:
1. To develop an instrument for measuring nursing role concepts.
2. To describe the "Ideal Nursing" concepts of psychiatric nurses at NIMH and to compare them with (a) "Ideal Nursing" concepts of varying degrees of psychiatric training and (b) other related professions' views of the "Ideal Nursing" concept e.g., administrative psychiatrists, psychotherapists, attendants etc.
3. To investigate the relationship between initial nursing-role concepts of staff members and (a) professional identifications, (b) nature and extent of training, and (c) experience.
4. To study the relationship between nature and extent of changes in nursing role concepts and (a) the initial discrepancy between the "prescribed" role and the individual's own role concept, (b) time of exposure to prescribed philosophy, (c) professional identification, and (d) training and experience.

Methods Employed: A 60 item Q-sample was devised. This Q-deck consists of statements describing attitudes and behaviors of psychiatric nursing personnel in dealing with psychotic patients. These were sorted periodically by all staff members of the Adult Psychiatry Branch, NIMH. The attitudes of staff members on each ward were compared with the "nursing role" concept of the ward administrator. Data were obtained from 23 psychotherapists,
Part A. Project Description (Cont'd)

5 ward administrators (psychiatrists) an experimental group of 19 psychiatric nurses and a control group of 19 psychiatric nurses. The study covers a period of two years during which each of the five administrators attempted to establish different treatment philosophies on wards treating chronic schizophrenic patients.

Major Findings:
1. Psychiatrists and nurses showed consistently different concepts of the preferred psychiatric nursing role.
2. Nurses initially show small but statistically significant modification of their nursing concepts in the direction of the new ward philosophy; however, these changes were unstable and disappeared in time.
3. The less acceptable a ward administrator's philosophy was to nurses initially, the less it was finally accepted by them even after 21 months of exposure to it.

Significance to the Program of Mental Health Research: The ward administrator who wishes to conduct research regarding the nature and effectiveness of a given "ward milieu" philosophy is dependent on the nursing staff for the faithful implementation of his ideas. This raised basic questions regarding the processes of accomplishing the goals of communication and acceptance by the nurses of the experimental philosophy. Our findings suggest that in selecting a ward staff, attention should be paid to the fact that (1) Training differences between psychiatrists and nurses may result in basic differences in expectation regarding nursing roles, and (2) The nurses' concept of her position may effectively limit the kinds of ward atmosphere that may be established.

Proposed Course of Project: Project has been completed and paper is being prepared for presentation at the Annual Meeting of the American Psychiatric Association in San Francisco, May 1958.

Part B included = No
Part A.

Project Title: Evaluation of the NIH Research Associates Training Program

Principal Investigator: Morris B. Parloff, Ph.D., Herman Turk, M.A.

Other Investigators: Donald S. Boomer, Ph.D., Allen T. Dittmann, Ph.D., Joseph H. Handlon, Ph.D., James Kincannon and Marvin Waldman, Ph.D.

Cooperating Units: Laboratory of Socio-Environmental Studies

Man Years (calendar year 1957): Patient Days (calendar year 1957):
Total: .85 None
Professional: .31
Other: .54

Project Description:

Objectives: To prove data permitting the directors of the Research Associate Program to evaluate:
   a) The extent to which the program meets the goal of communicating basic research philosophy and techniques to the medically trained investigator.
   b) The reactions and recommendations of trainees currently in the program.

Methods Employed:
   1. Open-end and structured interviews at regular intervals with the entire Research Associate group on individual career aspirations and reactions to the Program.
   2. Analysis of background data on the Research Associates to provide a framework for 1. above.

Major Findings: Cannot be reported as yet.

Significance to the Program of Mental Health Research: One of the basic problems of any research organization concerns the question of selection of personnel and provision of the appropriate setting to enhance the research capacity of the individual. This study
Part A. Project Description (Cont'd)

may provide some preliminary notions concerning the nature of the intricate relationships between 1) the capacities of the investigator-trainee, and 2) the attributes of the training setting in assisting the investigator to utilize his potentialities creatively.

Proposed Course of Project: Periodic data collection will extend over a period of about two years. A preliminary report will be made on or about November 13, 1957.

Part B included = No
Project Title: Attitude Changes in Nurse Trainees Subsequent to Psychiatric Training

Principal Investigator: Morris B. Farloff, Ph.D.

Other Investigators: Donald S. Boomer, Ph.D., Marvin Adland, M.D.

Cooperating Units: Chestnut Lodge, Rockville, Maryland

Man Years (calendar year 1957): Total: .58
Professional: .30
Other: .28

Patient Days (calendar year 1957): None

Objective:
1. To determine the "nurse-patient" attitude of nurse trainees prior to and following three months of psychiatric training.
2. To investigate the relationships among personality variables, conditions of training and nature and extent of changes subsequent to training.
3. To determine the relationship between "success" in psychiatric field work and personality and attitude measures.

Methods Employed: Before and after a 3 month field work placement at Chestnut Lodge, 62 nurse trainees described their concepts of "Ideal Nursing" of psychotic patients, completed the Welsh Anxiety and Repressions Scales, the Fascism Scale, and the Leary Interpersonal Checklist. The staff nurses were similarly tested. The nature of changes will be related to the personality measures available. Each student is graded on theory and practice. These grades will be related to (a) degree to which the students' final attitude approximates that of the staff nurses and (b) the degree of authoritarianism, "Anxiety and Repression".

Major Findings:
1. Nurses scoring high on the Fascism scale have significantly less "permissive" attitudes toward psychotic patients than do nurses low on the Fascism scale.
Part A. Project Description (Cont'd)

2. In the course of the training program, students' personality (as measured by the above instruments) show the following changes: significant decrease in "repression", a tendency to be less anxious, and significantly less authoritarian in their general attitudes.

3. Nursing Role Concepts are altered generally in the direction desired by the training staff with the exception that trainees reveal a significantly increased emphasis on "Physical Care". This latter finding may be interpreted as a response to covert training or an anxious reaffirmation of basic nursing concepts.

4. Nurses who subsequent to training decided to enter psychiatric nursing reveal a significant increase in emphasis on "Emotional Care" of the patients. This change is not found in nurses not desiring a psychiatric nursing placement.

5. No relationship was found between personality measures and success as measured by grades received.

Significance to the Program of Mental Health Research: Information regarding the selection and training of nursing personnel is of importance to NIMH in view of the heavy emphasis placed on the establishment of a therapeutic ward milieu to facilitate treatment of schizophrenic patients. Since the nurse is expected to play a critical role in this program, information which would facilitate appropriate selection and subsequent training would be useful.

Proposed Course of Project: These and other findings have been prepared for publication. A paper also is to be read at the American Psychiatric Association Annual Meeting in May 1958.
Part A.

Project Title: The Process of Change and the Communication of Value Systems in Psychoanalytic Therapy

Principal Investigator: Morris B. Parloff, Ph.D., Seymour Perlin, M.D.

Other Investigators: None

Cooperating Units: Laboratory of Clinical Sciences

Man Years (calendar year 1957): Total: .48
Professional: .20
Other: .28

Patient Days (calendar year 1957):
1 in-patient = 30 patient days
3 outpatients = 30 patient days

Project Description:

Objectives: To study the nature and direction of change in:
1) Value systems of the analysand, analyst and control analyst.
2) Perceptions of self and each other during the period of psychoanalysis (approximately 2 years).
3) Psychodynamics of the analysand.

Methods Employed: Data collection techniques include two Q Sorts that are administered to all participants periodically during the treatment period. One Q-Sort is descriptive of "Moral Values" and the other describes attitudes and behavior ranging from normal to pathological. A battery of psychological tests are administered at six month intervals to each of the patients.

Patient Material: Three psychoneurotic outpatients and one ambulatory schizophrenic patient began treatment with Dr. S. Perlin approximately 18 months ago and have continued to date. Each case is under the supervision of a different "control" analyst. These nine individuals are the subjects of the study.

Major Findings: No detailed analysis of the data has been undertaken since material is still being collected.

Significance to the Program of Mental Health Research: This study is consistent with the NIMH general interest in psychotherapy for it attempts to investigate some aspects of the psychotherapeutic process and the nature of changes effected in patients whose treatment is carried through to "completion". One focus of this
Part A. Project Description (Cont'd)

study takes up the popularly raised question that since effective therapy is an "attitude change" and "influence" procedure, the patient in addition to being assisted to modify his pathological perceptions may be influenced to take on the moral values of the therapist. Another area of significance to NIMH is the emphasis on describing the nature of the changes in the patients' personality over a period of extended intensive therapy.

Proposed Course of the Project: The final retesting of patients is currently underway. The data will be analyzed and presented for publication.

Part B included - No
Part A.

Project Title: Development of an Ego-Integration Conceptual System for Studying Psychotherapy

Principal Investigators: Donald S. Boomer, Ph.D., D. Wells Goodrich, M.D.

Other Investigators: None

Cooperating Units: Community Psychiatric Clinic in Rockville, Md., Washington Mental Health Clinic, Laboratory of Clinical Sciences, and Section on Personality Theory

Man Years (calendar year 1957): Patient Days (calendar year 1957):
Total: 1.72 Outpatients - 42 patient days
Professional: .80
Other: .92

Project Description:

Objectives: (1) Long-term: To develop a theoretical model and observational tools for the purpose of generating and testing a network of hypotheses about the conditions of personality change.
(2) Immediate: To organize a loose set of clinical-theoretical ideas and observations into a coherent model, as indicated above, and to determine the feasibility of observing certain critical changes in patient behavior during psychotherapeutic sessions.

We are concerned with the moment-to-moment level of ego-integration in the patient in his dealings with the therapist. We have conceptualized and hope to be able to identify in action four patterns of ego integration among which patients are presumed to shift during a therapy session. These have been carefully spelled out, but for the purpose of this report, brief descriptive summaries must suffice:

Defended (f) - The patient is controlling anxiety by his customary means, and is functioning at his characteristic level, involuntarily revealing from time to time, the ego-distorting aspects of his defensive functioning.
Partially defended (p) - Similar to f, but less stable and comfortable. Patient displays some readiness to move toward a suspension of his defenses, with concomitant premonitory anxiety.
Part A. Project Description (Cont'd)

Self observing (c.) - The widely-described "split ego" state in which the patient is monitoring his own behavior and considering simultaneously, or in rapid alternation, his feelings, his behavior and his defenses.

Decompensated (c.) - The overwhelmed ego: Anxiety is so high as to submerge defenses, disrupt some or all ego functions, and interfere with interpersonal and task-directed functioning. This may be a clear open panic state or a transitory disturbance, virtually unnoticeable unless reported by the patient.

Methods Employed: The investigators function together as a therapist-observer team, utilizing a one-way observation screen and a tape recorder for monitoring and recording the content of the interviews. Each investigator functions periodically as observer for the other's psychotherapy. In addition to the content of the hour, the observer's amplifying description of non-verbal events is electrically recorded.

These records provide a basis for regular discussion aimed at refining our concepts and operations. In addition to the theoretical work, we are exploring a set of verbal measures which we hope to use in the context of the ego-state model.

Our effort at present is primarily focused on two such measures: (1) Speech disruptions, and (2) The interpersonal locus of the patient's productions, gauged at the manifest level.

The speech disruption measure, adapted from Mahl, is a simple count of the incidence of a set of specified disruptions in speech, such as stutter, superfluous repetition, tongue-slip and the like. We are attempting to determine what effect rate of speech has on the incidence of these speech disruptions.

The interpersonal measure we are developing consists of a set of clearly defined categories for characterizing what or whom the patient is talking about, along a scale which ranges from things and abstractions through increasingly intense personal relationships to the relationship with the therapist.

It is our aim to use these measures, together with others yet to be developed, to define shifts in the patient's ego state.

Patient Material: Two female psychoneurotic outpatients are currently serving as our subjects. One is being seen twice weekly by Dr. Boomer; the other four times weekly by Dr. Goodrich. Briefer courses of therapy have been completed with three other patients. We contemplate the addition of from three to five more patients during the coming year.
Part A. Project Description (Cont'd)

Significance to the Program of Mental Health Research: The systematic investigation of relevant aspects of psychotherapy is a salient part of the program of NIMH. This project may contribute to this effort directly with substantive findings or indirectly with methodological and conceptual developments which can be utilized in other parallel investigations.

Proposed Course of the Project: This work, as currently envisaged, will continue throughout this year and well beyond. Some carefully controlled definitive work will be carried out during this year with regard to the incidence of speech-disruptions and the correlates of high and low incidence. The broader conceptual-theoretical work of formulating a model will also continue along the lines outlined above.

Part B included - No
Part A.

Project Title: Patterns of Responses on Psychodiagnostic Tests Yielded by Patients Suffering from Various Psychosomatic Diseases

Principal Investigator: Joseph H. Handlon, Ph.D.

Other Investigators: None

Cooperating Units: None

Man Years (calendar year 1957): Patient Days (calendar year 1957):
Total: 19
Professional: 11
Other: 8

Project Description:

Objectives:

a. General: To study the relationships between individual personality structure and susceptibility to the various psychosomatic diseases.

b. Specific: Preliminary to further study of this problem, a complete survey is to be made of the results of previous studies relating patterns of responses on psychodiagnostic tests to specific psychosomatic diseases.

Methods Employed: It will first be necessary to review quite exhaustively the findings of previous investigators who have attempted to relate various psychosomatic illnesses with specific responses on psychodiagnostic tests. After a careful compilation of such results, common patterns will be looked for. If such communalities are found, an attempt will be made to relate this with what is known about personality dynamics, and such results will serve as a base for further refinement of diagnostic work, particularly in relationship with preventative medicine.

Significance to the Program of Mental Health Research: It is hoped that the results of this study will shed some light on the etiology, general dynamics of, and the appropriate therapeutic interventions necessary for psychosomatic illness. It is also hoped that more refined diagnostic methods may be discovered.
Part A. Project Description (Cont'd)

which will make for more accuracy in the early discovery of the disease, as well as the specifying of personality types who would be likely to fall victim of such illnesses with an eye to preventing such an occurrence.

Proposed Course of the Project: An exhaustive search of previous studies which have used a variety of techniques upon a variety of disease entities will precede an analysis of the consistent patterns found in such studies. If such patterns are found and diagnostic instruments can be refined, further empirical validation of such findings will be attempted.

Part B. included - No.
Project Title: Development of Objective Measures of "Mental Health"

Principal Investigators: Joseph H. Handlon, Ph.D., Morris Rosenberg, Ph.D., Leonard Pearlin, Ph.D.

Other Investigators: None

Cooperating Units: Laboratory of Socio-Environmental Studies

Man Years (calendar year 1957): 11 Professional: 11 Other: 29

Project Description:

Objectives:
1. General: To develop techniques for the economic evaluation of "mental health" of large samples of subjects.
2. Specific: To apply the Guttman Scalogram Technique in the development of valid and reliable measures of "mental health".

Method Employed: An analysis will be made of questionnaire items of more or less known validity and reliability. In order to reduce the number of items administered to the respondent, the Guttman method of scalogram analysis will be employed to evaluate various existing personality scales of several well known questionnaires. Using those protocols which are at the present time available to us, the items will be processed to see if they lend themselves to the scalogram analysis. If a variety of items are found to scale, they will be further validated on selected samples of individuals, and results compared with other clinical tests.

Major Findings: No findings to report as yet. Project has just begun.

Significance to the Program of Mental Health Research: If the socio-environmental influence of a community upon the mental health of individuals living within that community is to be studied with any adequacy, it will be necessary to develop techniques that lend themselves to such a study. So far there have been few attempts
Part A. Project Description (Cont'd)

to develop methods by which large segments of the population can be sampled and evaluated. If such methods can be devised, it will mean that much important information heretofore not available to investigators who are interested in studying in an objective fashion community health problems will now be available.

Proposed Course of the Study: After a statistical analysis of the data now available at NIMH, the results will determine whether such previously used measures lend themselves to scalogram analysis. If satisfactory scales can be derived, they will be checked out on other samples which will be made available for this purpose. It is proposed that other questionnaires having to do with psychic health as well as disease will be evaluated as well. The advisability of the development of new scales will also be considered.

Part B included = No

- 156 -
Part A.

Project Title: An Analysis of Interpersonal Communication Patterns Within Families of Schizophrenics and Non-Schizophrenics in Quasi-Experimental Group Situations

Principal Investigator: Joseph H. Handlon, Ph.D.

Other Investigators: Morris B. Parloff, Ph.D., Donald S. Boomer, Ph.D., Marvin Waldman, Ph.D., Lyman Wynne, M.D.

Cooperating Units: Adult Psychiatry Branch, Laboratory of Socio-Environmental Studies

Man Years (calendar year 1957): Total: .30
Professional: .22
Other: .08

Project Description:

Objectives: There is evidence to suggest that there may be interpersonal communication patterns which are unique to families one of whose members is a schizophrenic. It will be the purpose of this study to attempt to demonstrate these assumed differences in structured, quasi-experimental group situations which lend themselves readily to objective observational and measurement techniques.

Method Employed: Making use of previous studies, techniques will be developed which will permit accurate measures of interpersonal communication patterns in an observed group situation. At the present stage of planning several techniques suggest themselves, including the use of quasi-groups where, unknown to the subjects, interpersonal communication can be manipulated systematically by the experimenter. The advantage of such observational methods of evaluating intra-family behavior is that it lends itself to objective, reliable measures suitable for comparative studies, while at the same time preserving in large measure the natural group dynamics. Both families of schizophrenics as well as control groups of various normal and non-schizophrenic psychiatric entities will be studied. Relationships between the findings in the experimental group situation and 1) discovered
Part A. Project Description (Cont'd)

patterns on diagnostic tests of personality; 2) personality dynamics as gleaned from individual and/or group psychotherapy; and 3) where appropriate, ward behavior, will be examined.

Significance to the Program of Mental Health Research: If it is the case that the intra-family dynamics play a crucial role in the course of schizophrenia, then a careful study of these dynamics under controlled conditions would seem to be profitable. It will be particularly important to determine whether such consistent intra-family communication patterns as are found are really unique to families of schizophrenics, or whether they are to be found in non-schizophrenic families as well. If found in both schizophrenic and non-schizophrenic, is there a difference in degree? A correlative question is that of whether such patterns as may be found are a result of having a mentally disturbed member in the family, or whether they are an important contributing factor in the actual development of schizophrenia.

Proposed Course of Project: After an exhaustive review of the various techniques which have been employed in the experimental study of group processes, appropriate methods will be tried out in pilot studies with a variety of groups. Once techniques have been perfected, use will be made of the families of schizophrenics and others who are in-patients at NIH as well as normal groups. Findings will then be correlated with other psychologically relevant material gleaned from diagnostic tests, group and individual therapy, and ward behavior.
Project Title: Value Changes in Psychiatric Nursing Trainees

Principal Investigator: Herbert C. Kelman, Ph.D.

Other Investigators: Donald S. Boomer, Ph.D.

Cooperating Units: None

Man Years (calendar year 1957): Total: .63
Professional: .17
Other: .46

Patient Days (calendar year 1957): None

Project Description:

Objectives: The purpose of this project is to study some of the factors that are related to changes in attitudes, values, and role conceptions on the part of student nurses undergoing psychiatric training. Of particular interest are those values which relate to patient care and sensitivity to the patient’s needs, as well as to sensitivity in interpersonal relations in general. Specifically, the project will be concerned with the effects on value change of (1) certain specified personality predispositions of the student nurses, and (2) variations in the training method employed. In measuring the effects of the training, the study will focus not only on amount of change, but also on level of change: an attempt will be made to measure changes in public attitudes, in behavior, and in general values. This study represents an integration and elaboration of two previous studies reported in 1955: NIMH 118(C) and NIMH 128(C).

Methods Employed: As presently planned, the study will involve experimental manipulation of one part of the training program, and informal observation of the training program in general. In order to measure relevant personality predispositions, a variety of techniques will probably be used. These may include standard personality tests, interviews, and special laboratory situations (probably of a quasi-group nature). Both the variations in the training procedure and the personality
Proposed Course:
The resignation of Dr. ...

Part B included - NO
Part A.

Project Title: Validation of Specificity Theory of Psychosomatic Disease

Principal Investigator: Herbert C. Kelman, Franz Alexander, Morris Stein

Other Investigators: None

Cooperating Units: None

Man Years (calendar year 1957): Patient Days (calendar year 1957):
Total: .25
Professional: .17
Other: .08

Project Description:

Objectives:
1. To validate hypotheses about specific personality dynamics, life history, and onset situations related to each of seven psychosomatic syndromes.
2. To develop methods for such validation and determine the effects of degree of psychiatric sophistication on results obtained.

Methods Employed: Detailed checklists were filled out after reading of transcribed anamnesic interviews with psychosomatic patients, from which all medical information had been deleted. From those, diagnoses will be derived and checked against presenting symptoms.

Subjects Used: Two groups of judges completed the checklist -- a group of secretaries, unacquainted with psychiatric concepts and the specific hypotheses; and a group of graduate students in psychology, who in addition were informed of the specific hypotheses. Diagnoses made by a group of psychoanalysts, who read the same case material but did not use the checklist are available for comparison.

Major Findings: (1) In general, the study shows that it is possible to isolate factors in a patient's life history and personality dynamics which are related to the specific psychosomatic syndrome which he develops. (2) The data support three of the six personality
Part A. Project Description (Cont'd)

and life history patterns which were studied: patients who develop peptic ulcer, bronchial asthma and thyrotoxicosis tend to be characterized by the psychological patterns which the investigators hypothesized. The patterns for neurodermatitis and essential hypertension tended in the hypothesized direction but were not statistically significant. The hypotheses in the case of ulcerative colitis were clearly not supported.

Significance to the Program of Mental Health Research: Treatment of psychosomatic patients depends on an understanding of the personality and conflicts of the patient. This study aims to get some indication of the validity of certain hypotheses about specific syndromes. The methodological part of the study should give some information on the reliability of various ways of collecting relevant data.

Proposed Course of the Project: This project has been terminated due to the resignation of Dr. Kelman.

Part B included - No
Part A.

Project Title: Processes of Acceptance of Social Influence

Principal Investigator: Herbert C. Kelman

Other Investigators: None

Cooperating Units: None

Man Years (calendar year 1957): Total: .50
                                          Professional: .17
                                          Other: .33

Patient Days (calendar year 1957): None

Project Description:

Objectives: To distinguish three processes whereby influence is accepted -- compliance, identification, and internalization and to show that these are produced by different motivational conditions and have different subsequent histories.

Methods Employed: Several different tape recorded communications were used to create different perceptions of the communicator's power and different motivations for acceptance of influence. The effects of these on an area of social attitudes were measured through repeated questionnaires.

Subject Used: College students

Major Findings: Attitudes accepted through compliance (communicator has means-control) tend to be expressed only under conditions of surveillance by the communicator. Attitudes accepted through identification (communicator is attractive) tend to be expressed only under conditions of salience of the communicator. Attitudes accepted through internalization (communicator is trustworthy) tend to be expressed regardless of surveillance or salience of the communicator.

Significance to the Program of Mental Health Research: The therapeutic situation can be regarded as a situation of social interaction and the therapeutic process as a product of social influence.
Part A. Project Description (Cont'd)

It is through these interpersonal relationships that the patient is able to modify his values, attitudes, and role expectations. Therefore, the development of a general theory of social interaction and influence should increase our understanding of the therapeutic process. The present study can contribute to our understanding of the conditions under which therapeutic changes will be lasting and integrated with the patient's values and the conditions under which they will be superficial and of short duration. In addition, it can be useful for the development of programs of public education on mental health.

Proposed Course of the Project: A detailed report of the study and of the theory underlying it has been written. This report will be revised and expanded for publication as a monograph. This project has been terminated due to the resignation of Dr. Kelman.

Part B included - Yes
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:

Kelman, Herbert C. *Social Influence and Personal Beliefs: A Theoretical and Experimental Approach to the Study of Behavior Change* (To be published by Wiley and Sons, Inc., New York)


Honors and Awards relating to this project:

Awarded the $1,000 Socio-Psychological Prize of the American Association for the Advancement of Science, New York City, December, 1956 for his essay entitled, "Compliance, Identification, and Internalization: A Theoretical and Experimental Approach to the Study of Social Influence."
NATIONAL INSTITUTE OF MENTAL HEALTH

Clinical Investigations
Laboratory of Clinical Science--Office of the Chief

BUDGET SHEET

Estimated Obligations for FY 1958

Total: $151,849
Direct: $107,067
Reimbursements: $44,782

Projects included: M-CS-OC(C) 1 through M-CS-OC(C) 4
Part A.

Project Title: Biological Studies in Schizophrenia

Principal Investigator: Seymour S. Kety

Other Investigators: See individual projects.

Cooperating Units: See individual projects in the Laboratory of Clinical Science, NIMH, as follows: Office of the Chief, Serial Nos. M-CS-OC(C)-2, 3, and 4; Section on Medicine, Serial Nos. M-CS-M(C)-1 and 4; Section on Psychiatry, Serial Nos. M-CS-Ps(C)-2 and 4; Section on Cerebral Metabolism, Serial Nos. M-CS-CM-1, 5, 6, and 7; Section on Drug Evaluation, Serial No. M-CS-DE-1; and Section on Biochemistry, Serial No. M-CS-B-4 and 5.

Man Year (calendar year 1957): Patients Days (calendar year 1957):

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Project Description:

Objectives: To direct and coordinate a multidisciplinary program of biochemical, pharmacological, and physiological studies in schizophrenia and their correlation with psychological and psychiatric aspects of the disease.

a. Studies on amino acid metabolism
b. Studies on the fate and effects of epinephrine
c. Evaluation of reported biological abnormalities

Methods Employed: Selected populations of schizophrenics and normal controls have been established and are maintained under controlled conditions of normal diet, activity and management. Three general techniques are employed for studies of a particular substance in both populations: 1) examination of its blood level or urinary excretion and their correlation with psychological and psychiatric observations; 2) examination of the psychological, biochemical, and physiological effects of the
Project Description (continued):

administration of measured amounts of the substance to permit assessments of differences in the handling or effects of the substance in the two groups; and 3) the administration of radioactively tagged substances and examination of blood levels and urinary output of all radioactive products to permit qualitative and roughly quantitative estimates of its various metabolic pathways.

Major Findings: The program is relatively recent in its inception. Criteria for the selection of patients have been established and the sample drawn up from an examination of several thousand state hospital charts. Techniques have been adapted for the effective fractionation of metabolic products in blood and urine, and animal experiments are in progress to permit determination of safe doses of particular radioactive compounds in man. Specific findings are reported in the component projects.

Significance to Mental Health Research: Many positive findings relating to biological abnormalities in schizophrenia have not been subjected to well controlled and critical evaluation. There are numerous reasons which suggest abnormalities in the metabolism of amino acids or certain amines as essential factors in some forms of schizophrenia. This program offers a means of evaluating such hypotheses.

Proposed Course of Project: The program is planned for several years' duration.

Part B included: Yes
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:


Honors and awards relating to this project:

Dr. Seymour S. Kety:

Elected to the Council of the International Collegium of Psychopharmacology.
Elected to membership in American Psychopathological Society.
Appointment to Committee on Research in Dementia Praecox, Supreme Council 33° Scottish Rite, Northern Masonic Jurisdiction.
Address to the Harvey Tercentenary Congress, London, June 1957.
Part A.

Project Title: Comparison of the Excretion Patterns of Metabolites of Aromatic Amino Acids by Normal Subjects and Schizophrenic Patients

Principal Investigator: Elwood H. Labrosse

Other Investigators: Jay D. Mann

Cooperating Units: None

Man Years (calendar year 1957): Patient Days (calendar year 1957):

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Project Description:

Objectives: Numerous investigators have described quantitative differences in the excretion of urinary phenolic acids between normals and schizophrenic patients. In many cases these studies have been so incompletely reported that they could not be repeated in exactly the same manner or they had insufficient numbers or inadequate controls. Because of the close biochemical relationship of the neurohumors, such as epinephrine and norepinephrine and of such compounds as serotonin, to the aromatic amino acids, the metabolism of the latter is important in mental function—this has been clearly shown in phenylpyruvic oligophrenia in which a disturbance in the hydroxylation of phenylalanine to tyrosine is consistently associated with mental deficiency. The objective of this investigation will be to establish whether there is a significant difference in the metabolism of aromatic amino acids by normals and by schizophrenic patients. If a difference actually is found to be present, it will then be possible to set up further experiments which will elucidate the biological relationship between metabolism and schizophrenia.
Project Description (continued):

Methods Employed: The normal subjects and schizophrenic patients will be given identical diets in addition, following a double-blind technique; half of each group will be given a loading dose of phenylalanine, tyrosine or tryptophane. Urine specimens will be collected over known time periods and replicate portions of each urine specimen will be analyzed using quantitative paper chromatographic methods to analyze numerous urinary metabolites of the aromatic amino acids. These data will be analyzed statistically to determine whether there is a significant difference in the excretion of these metabolites between the normals and the schizophrenics.

Major Findings: This project is just getting started and no major findings have yet been obtained.

Significance to Mental Health Research: If a significant difference between normals and schizophrenic patients were found, it would be a major breakthrough in the understanding of mental illness and would provide a point of entry for elucidation of the biochemical factors in mental illness and thereby lead to a more rational and effective therapy.

Proposed Course of Project: To begin the loading experiment as soon as equipment, supplies, and technical assistance can be obtained. To combine with or extend this study to include administration of C\(^{14}\)-labeled amino acids.

Part B included: No
Part A.

Project Title: Study of the Metabolites of Epinephrine and Norepinephrine in Human Body Fluids

Principal Investigator: Elwood H. LaBrosse

Other Investigators: Seymour S. Kety, Julius Axelrod

Cooperating Units: None

Man Years (calendar year 1957): Patient Days (calendar year 1957):

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<td>0.25</td>
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Project Description.

Objectives: To investigate the metabolites of epinephrine and norepinephrine in the urine and in the blood in the approach to studies of the in vivo metabolism of these important neurohumors in normal and mentally ill subjects.

Methods Employed: Treatment of the urine with β-glucuronidase, followed by extraction and paper chromatography of the extracts were used in the search for these metabolites. This study will be greatly facilitated when the tritium labeled epinephrine becomes available, at which time the total radioactivity in the urine and the relative amounts in various constituents will be determined.

Major Findings: This project has just begun and there are no significant findings to report at this time.

Significance to Mental Health Research: Both epinephrine and norepinephrine are well known as neurohumors and have been found in the brain as well as in the peripheral nervous system. Because of this fact an understanding of their metabolism would facilitate an evaluation of their role in normal function of the nervous system and in mental disease.
Project Description (continued):

**Proposed Course of Project:** It is planned to continue this investigation and to study the labeled metabolites after the intravenous injection of tritium labeled epinephrine.

Part B included: No
Part A.

Project Title: Studies of the interrelationships of the nervous and circulatory systems.

Principal Investigator: P.V. Cardon, Jr., M.D.


Cooperating Units: Clinical Investigations, NIMH; Lab. of Cellular Physiology and Metabolism, NHI

Man Years (Calendar year 1957) Patient Days (calendar year 1957)
Total: 2 1/3 70
Professional: 1
Other 1 1/3

Project Description:

Objectives: 1. To clarify the nature of the changes which occur in the circulatory system in association with changes in various parameters of central nervous system function such as attitudes, feeling states, modes of interpersonal reaction, and psychomotor performance.

2. To develop and standardize reproducible, simple, and non-traumatic methods for the assessment of such circulatory changes.

Methods Employed: Circulatory changes are assessed by the following methods: Pulse rate, blood pressure (auscultatory or direct arterial measurement), ballistocardiograph, impedance plethysmograph.

More studies this year involved comparison between groups (i.e., normal vs. schizophrenic patients) rather than measurement of changes in the same individual. Four preliminary studies of the effects of infusing epinephrine into normal and schizophrenic subjects have been done in collaboration with six other investigators in the laboratory. One psychoneurotic out-patient was studied immediately before and after therapeutic interviews for 17 weeks (Dr. Goodrich). The number of normal subjects in whom plasma unesterified fatty acid (UFA) was measured before and after a sham...
Traumatic procedure was expanded to 18 (Dr. Gordon). The circulatory effects of amphetamine, phenobarbital, and meprobamate were studied in normal subjects (Dr. Kornetsky). Comparison of the impedance plethysmograph and Na\textsuperscript{24} methods of estimating leg blood flow was completed (Dr. Sokoloff). Induction of circulatory changes with structured interviews has been abandoned for the time being because of the data-reduction problem and the resignation of the participating psychiatrist (Dr. J.M. Scher).

Patient Material: Patients on 4-W and 2-W of the Clinical Center.

Major Findings: (Findings enumerated include results of analyzing some data collected in 1956).

As a group, schizophrenic men tend to have smaller ballistocardiographs than do normal men. Other circulatory variables studied are not different. Within the schizophrenic sample, variables studied have not been found so far to correlate with behavioral, EEG, or biochemical sub-groupings.

In the studies of the acute effects of a variety of centrally acting drugs, chlorpromazine significantly increased pulse rate and meprobamate decreased ballistocardiograph amplitude.

On the basis of comparison with the Na\textsuperscript{24} clearance method, the impedance plethysmograph is not a good method for estimating relative change in limb blood flow.

Acute anxiety usually causes an increase in plasma UFA.

Significance to Mental Health Research: Problems to which these studies may prove pertinent include: tranquilizing drugs, anxiety states, schizophrenia, neurocirculatory asthenia, essential hypertension, and coronary heart disease.

Proposed Course of Project: Continue studies of the types reported on the same relatively small and flexible scale.

Part B included: Yes
Part B.

NATIONAL INSTITUTE OF MENTAL HEALTH

Clinical Investigations
Laboratory of Clinical Science--Section on Medicine

BUDGET SHEET

Estimated Obligations for FY 1958

Total: $172,054
Direct: $56,314
Reimbursements: $115,740

Projects included: M-CS-M(C) 1 through M-CS-M(C) 6
Part A.

Project Title: Behavioral and biochemical correlates of the electroencephalogram (EEG) in schizophrenic patients.

Principal Investigators: Roger K. McDonald, M.D., William Pollin, M.D., Frederick Snyder, M.D., Robert R. Butler, M.D., and Edward V. Evarts, M.D.

Other Investigators: Bonnie Peacock

Cooperating Units: None

Man Years (calendar year 1957) 5/6

Patient Days (calendar year 1957): 731

Project Description:

Objectives: A variety of biochemical studies in schizophrenic patients have yielded data whose mean does not differ significantly from the mean of a normal population, but whose variability exceeds that of the normal population. So far, few attempts to determine the relationship between these variable biochemical data and behavioral or biological processes have been made. The present project represents a preliminary effort to determine the degree to which one form of biological activity (the EEG) may be related to a number of biochemical and behavioral measures.

Methods Employed: (A) Patient Selection: Approximately 150 white male schizophrenic patients between the ages of 20 and 40 were selected from the population of the Springfield and Spring Grove State Hospitals. Care was taken to exclude any patients with organic brain disease or mental deficiency. Tracings of occipital electrical alpha activity were obtained in these patients. The EEG records were divided into three groups according to whether they showed high, low, or intermediate amounts of alpha activity. A number of patients in each of these categories was admitted to the Clinical Center. All patients who were selected for admission to the Clinical Center were evaluated clinically. Only those patients with clearly schizophrenic disorders were admitted. These patients had been hospitalized for one or more years.
(E) EEG Studies: Patients were examined electroencephalographically at the time of admission and at weekly intervals thereafter. Records were analyzed with respect to per cent alpha so that a quantitative score descriptive amount of alpha would be available for correlation with behavioral and biochemical variables. Studies of photic activation of the EEG were also carried out.

(C) Pharmacologic and Electromyographic Studies: The attempt was made to test the hypothesis that the percentage of alpha activity is a reflection of the degree of arousal of the organism by measuring several physiological indices which are reputed to be correlated with the level of anxiety, i.e., the sedation threshold and surface muscle activity. The sedation threshold is obtained by determining the amount of intravenous sodium amytal which is necessary to produce the specific electroencephalographic change associated with the effect of barbiturates on cortical rhythms. Muscle activity was measured by surface electromyographic methods from the various parts of the body to provide an objective indication of tension in individual subjects.

(D) Behavioral Studies: Patients were seen for recorded, observed evaluation interviews shortly after their admission. Their EEG characteristics were unknown to the evaluating psychiatrists at that time. Data obtained were used for final confirmation of the diagnosis of schizophrenia, and for the purpose of making independent rankings of 19 personality variables which, on the basis of prior work, were thought likely to relate to per cent alpha. These rankings fell into five major categories: Ego intactness, reality contact, reality distortion, affects and activity. Two hypothesized profiles using these rankings were constructed. These profiles were based on work from the literature, and were designed to differentiate the high from the low alpha. Predictions were made as to which of the two categories each patient would be in. After comparison of the EEG characteristics and psychiatric findings, patients were re-evaluated. Continuing ward observations were made by psychiatric and nursing personnel. A modified version of the Lohr scale, and various additional experimental techniques were employed for rating ward behavior.

(E) Biochemical Studies. The laboratory methods employed in this study are described under the project entitled, An Evaluation of Certain Reported Biochemical Differences Between Schizophrenic and Non-psychotic Subjects.

Major Findings:

(A) Correlations Between EEG and Behavior. The relationship between psychiatric rankings and behavioral ratings, on the one hand, and per cent alpha on the other was not statistically significant. Re-evaluation after comparison of EEG and psychological data has led to a reformulation of the hypothesized clinical picture which may be related to high or low alpha characteristics.
No consistent relationship was found between the percentage alpha and the sedation thresholds of the patient group, nor could the latter measure be correlated with psychiatric judgments concerning apparent anxiety in the subjects. The results were in keeping with previous provocative reports that in schizophrenics there is no clear-cut relationship between the sedation threshold and behaviorally manifest anxiety, as there is in neurotic patients or normal controls. Neither was there a consistent relationship between a global measure of muscle tension and the alpha index. The data suggest, however, that there may be such a relationship with muscle tension in certain areas of the body, notably the forehead and periorbital muscles. This possibility is still being explored.

(B) Correlations Between EEG and Biochemical Measures. Of the variety of biochemical measures which was carried out, only red blood cell glutathione (GSH) was significantly correlated with per cent alpha in the schizophrenic patients. The mean GSH was 76.6 mg. in patients with high alpha and 63.0 mg. in patients with low alpha.

Initial observations suggesting differences in blood levels of ascorbic acid between the high and low alpha groups appeared to be the result of differences in dietary intake of ascorbic acid. Evidence for this belief rests on the complete similarity of blood levels of ascorbic acid in the two groups following an ascorbic acid loading-deprivation experiment.

Adrenaline oxidation, which has been shown to be a function of ascorbic acid and copper levels in the blood, did not differ in the two groups. Likewise, serum oxidation of paraphenylenediamine, which is a function of serum copper, did not differ in the two groups.

Significance to Mental Health Research:

(A) Biochemical Findings. The positive correlations between blood glutathione and per cent alpha is of considerable interest in view of the observations of some previous investigators that blood glutathione is depressed in certain forms of mental illness. The present study does not demonstrate such differences between normals and schizophrenics taken as a group, but does indicate that there is a suggestive relationship between blood glutathione and at least one measure of central nervous system activity.

(B) Behavioral Findings. Thus far, no significant clinical correlates of high or low alpha characteristics have been established.
Proposed Course of Project:

(A) Biochemical. The small size of the present sample would make it mandatory that the observations on blood glutathione and EEG be extended to more schizophrenic patients. In addition, studies will be carried out to determine the relation of blood glutathione to the EEG in a normal population.

(B) Behavioral. High and low alpha schizophrenic patient groups at two nearby State Hospitals will be psychiatrically evaluated, without knowledge of which EEG grouping each patient belongs to. On the basis of the study of the present patient group, predictions as to EEG characteristics will be made to test the significance of suggested clinical correlates of alpha per cent.

Part B included: No
Project Title: Qualitative intraspecies variations in human serum cholinesterase.

Principal Investigator: Franklin T. Evans, M.D.

Other Investigators: Roger K. McDonald and Raymond W. Patrick

Cooperating Units: None

Man Years (calendar year 1957) Patient Days (calendar year 1957)
Total: 1 60
Professional: 5/12
Other: 7/12

Project Description:

Objectives: To examine the possibility that qualitative differences in serum cholinesterase exist between different human subjects.

Methods Employed: The rate of hydrolysis of B-carbonaphthoxycholine and B-naphthyl acetate by human serum, and the effect of calcium and magnesium ions on this rate have been studied by the colorimetric method of Ravin, Tsou and Seligman. The rate of hydrolysis of acetylcholine by human serum has been studied by the colorimetric method of de la Huerga, et al.

Method for studying individual variation in human serum cholinesterase. Various concentrations of calcium and magnesium, with and without eserine, were added to the sera of a group of patients, and the resultant hydrolytic activity of the sera was determined individually.

Patient Material: Normal male and female volunteers and schizophrenic males.

Major Findings: Presently available data do not justify definite conclusions regarding intraspecies variations of cholinesterase at this time. The preliminary findings do suggest that further investigation of the effect of calcium and magnesium on cholinesterase is warranted.
Significance to Mental Health Research: Although the physiologic substrate of serum cholinesterase is at present unknown, recent evidence has shown that inhibition by the serum-type cholinesterase in isolated brain preparations results in a so-called arousal response on electroencephalogram. In addition, a number of psychotomimetic drugs are known to inhibit this enzyme. These facts suggest that a more careful exploration of the nature of this enzyme may ultimately clarify its possible role in central nervous system activity.

Part B included: No
Effect of morphine and nalorphine on plasma hydrocortisone levels.

Principal Investigator: Roger K. McDonald, M.D.

Other Investigators: Franklin T. Evans, M.D., Raymond W. Patrick, and Virginia K. Weise

Cooperating Units: None

Man Years (calendar year 1957) Patient Days (calendar year 1957)
Total: 1 1/6 128
Professional: 2/3
Other: 1/2

Objectives: To determine whether morphine and nalorphine suppress ACTH release in man.

Laboratory Methods: Plasma hydrocortisone concentrations were determined by the method of Peterson et al.

Methods Employed: The hourly plasma hydrocortisone levels from 8 a.m. to 1 p.m. were determined on a group of normal subjects on one day following placebo injections, on another day following morphine injections, and on a third day following nalorphine. The second design employed in this study consisted of determining the effect of morphine on the large rise in plasma hydrocortisone concentration which characteristically occurs between 4 a.m. and 8 a.m. In this design a group of normal subjects received on one night oral pentobarbital and at 3 a.m. a subcutaneous injection of morphine sulfate. At 6 a.m., 7 a.m., and 8 a.m. fasting blood samples were drawn for a comparison of plasma hydrocortisone levels with levels on other mornings when either nembutal or placebos were given at the scheduled times.

Patient Material: Normal male and female volunteers were used exclusively.

Major Findings: In the first part of the study both morphine and nalorphine produced a significant depression of the plasma hydrocortisone level which occurred at 11 a.m. and continued through 1 p.m. In the second part of the study morphine blocked the morning rise in plasma hydrocortisone concentration.
Significance to Mental Health Research: These observations indicate that morphine and nalline suppress significantly the release of ACTH by the anterior pituitary gland. Since the action of morphine and nalline is most likely on the central nervous system it would appear that the normal control of ACTH release in man is under central nervous system control.

Proposed Course of Project: The present approach has provided an answer to the question of the interrelationship between morphine, nalorphine administration and ACTH release. The project will not be continued unless new approaches become apparent.

Part B included: No
Part A.

Project Title: An evaluation of certain reported biochemical differences between schizophrenic and non-psychotic subjects.

Principal Investigator: Roger K. McDonald, M.D.

Other Investigators: Virginia K. Weise, Franklin T. Evans, M.D., and Raymond W. Patrick

Cooperating Units: Springfield State Hospital, Sykesville, Md.
St. Elizabeths Hospital, Washington, D.C.

Man Years (calendar year 1957) Patient Days (calendar year 1957)
Total: 1 1/4 235
Professional: 2/3
Other: 7/12

Project Description:

Objectives: To determine the plasma copper and ascorbic acid levels, the red blood cell reduced glutathione levels and the oxidizing capacity of serum and plasma for N-N’dimethyl para-phenylenediamine (DPP), p-phenylenediamine and adrenaline in schizophrenic and non-psychotic subjects. These various parameters have been reported to be abnormal in schizophrenic patients.

Methods Employed: Laboratory methods included copper analysis by the method of Cubler et al., ascorbic acid analysis by the method of Roe, red blood cell glutathione determination by the method of Grunert and Phillips and the serum oxidation of DPP by the method of Akerfeldt, of p-phenylenediamine by the method of Abood and of adrenaline using the method of Leach et al.

Patient Material: Schizophrenic patients were studied at the Clinical Center, St. Elizabeths Hospital and Springfield State Hospital. Normal male and female volunteer subjects were used as controls.

Major Findings: No significant difference was found between the serum copper and red blood cell glutathione values and the serum oxidation rates for DPP and p-phenylenediamine for schizophrenic and control subjects. The serum ascorbic acid levels were lower in the schizophrenic group, but this was shown to be a dietary phenomenon. Adrenaline oxidation was more rapidly oxidized by plasma from schizophrenic subjects, but this was shown to correlate highly with the plasma ascorbic acid levels. The latter observation suggests that abnormally high dye and adrenaline oxidation rates found in schizophrenics are simply a result of low plasma ascorbic acid levels resulting from low dietary intake.
Significance to Mental Health Research: This study falls into the over-all laboratory approach to biological studies in the psychoses. It is hoped that this approach will be of aid in better understanding the complex phenomena of mental disease.

Proposed Course of Project: Certain aspects of this project are continuing to provide a more critical evaluation of "peripheral" biochemical findings and central nervous system function.

Part B included: No
Project Title: The relationship between endogenous antidiuretic hormone activity and ACTH release in man.

Principal Investigator: Roger K. McDonald, M.D.

Other Investigators: Henry N. Wagner, Jr., M.D. and Virginia K. Weise

Cooperating Units: Laboratory of Kidney and Electrolite Metabolism, NIH

Jan Years (calendar year 1957) Patient Days (calendar year 1957):
Total: 3/4 150
Professional: 5/12
Other: 1/3

Project Description:

Objectives: To determine if the endogenous release of antidiuretic hormone causes ACTH release.

Methods Employed:

Laboratory Methods: 1. Determination of plasma hydrocortisone concentration by the method of Peterson et al.

2. Urine osmolality determined by freezing point depression.

Method of studying interrelationship of antidiuretic hormone and ACTH release.

Stimuli used for production of either antidiuretic hormone or ACTH release consisted of water deprivation, intravenous injection of hypertonic saline, intravenous injection of insulin and nicotine, intramuscular injection of mecholyl and hand immersion in ice water. At appropriate intervals urine and blood were collected for analysis of plasma hydrocortisone concentrations and antidiuretic hormone activity.
Patient Material: Normal male and female volunteers.

Major Findings: The experiments demonstrate that antidiuretic hormone and ACTH release can occur independently of each other and therefore antidiuretic hormone is not the neurohormone causing ACTH release.

Significance to Mental Health Research: The ACTH release associated with various stress is a study of this problem pertinent to the inter-relationship between stress and bodily function. This study disproves one of the current hypotheses employed in explaining the relationship between the central nervous system and endocrine control.

Proposed Course of Project: This particular project has provided the answer to the problem examined and is not being studied further.

Part B included: Yes
Part B.

Publications.


Other Publications.

Project Title: Morphine suppression of pitressin-induced ACTH release in man.

Principal Investigator: Roger K. McDonald, M.D.

Other Investigators: Virginia K. Weise, Raymond W. Patrick, and Franklin T. Evans, M.D.

Cooperating Units: None.

Man Years (calendar year 1957) Patient Days (calendar year 1957)
Total: 2 110
Professional: 2/3
Other: 1 1/3

Project Description:

Objectives: Pitressin (vasopressin) has been postulated to be the neurohormone responsible for directly stimulating ACTH release from the anterior pituitary gland. In addition to causing ACTH release the intravenous administration of pitressin in human subjects is accompanied by unpleasant subjective symptoms which, in themselves, could be sufficiently stressful to cause ACTH release. This study is designed to determine whether pitressin-induced ACTH release in man can be suppressed by morphine, a drug which has known central nervous system action.

Methods Employed: Plasma hydrocortisone concentrations were determined by the method of Peterson et al. The levels obtained were assumed to be an indication of ACTH activity.

Patient Material: Normal volunteer subjects were employed in this study.

Major Findings: In normal human subjects the ACTH release resulting from the intravenous injection of pitressin is significantly reduced by morphine premedication. Morphine has no suppressive effect on adrenocortical responsiveness to intravenously administered ACTH.

Significance to Mental Health Research: This study provides further evidence against the hypothesis that antidiuretic hormone acts directly on the anterior pituitary gland to produce ACTH release. It is part of the overall program for evaluating hypothalamic-hypophysial interrelationship which is concerned with the individual's adaptation to frequently changing life situations.
Proposed Course of Project: No direct continuation of this project is contemplated at the present time.

Part B included: No
Estimated Obligations for FY 1958

Total: $196,226
Direct: $69,467
Reimbursements: $126,759

Projects included: M-CS-P(C) 1 through M-CS-P(C) 5
Part A.

Project Title: An attempt to differentiate between the thinking disorder found in schizophrenics and that found in patients with the diagnosis of chronic brain syndrome.

Principal Investigator: Irwin Feinberg, M.D.

Other Investigators: Edward V. Evarts, M.D.

Cooperating Units: St. Elizabeths Hospital, Washington, D.C.

Patient Days (calendar year 1957): 2/3

Total: 2/3

Professional: 2/3

Other: None

Project Description:

Objectives: 1. To characterize more precisely the nature of the thinking disorder found in schizophrenia.

2. To devise a test which will distinguish the thinking of schizophrenics from that of patients with chronic brain syndrome.

Methods Employed: Our starting hypothesis is that schizophrenics may have a selective difficulty in recognizing relationships and that, in a test comparing the ability to recognize identities and relationships, organics may perform equally poorly on both but that schizophrenics will be significantly worse on the latter.

Patient Material: Patients hospitalized in the William A. White Building of St. Elizabeths Hospital with the diagnosis of schizophrenia and those in other buildings with the diagnosis of chronic brain syndrome.

Major Findings: None at present.

Significance to Mental Health Research: A more accurate description of this basic aspect of the disease process will be of value in the assessment of induced model-psychoses and of the effect of various treatment procedures.

Proposed Course of Project: Testing will be started shortly in an attempt to evaluate the above hypothesis. The literature in the field is being reviewed.
Project Title: The effects of a variety of centrally acting drugs on intellectual, motor, and perceptual behavior in normal subjects.

Principal Investigator: Conan Kornetsky, Ph.D.

Other Investigators: Thomas Vates, M.D., Mary Lee Geisser, and Edith Kommen

Man Years (calendar year 1957):
- Total: 1 1/3
- Professional: 1/3
- Other: 1

Patient Days (calendar year 1957): 630

Project Description:

Objectives: 1. To determine what differences may exist in the psychological effects of opiates, tranquilizing drugs, barbiturates, psychotomimetics, and alcohol.

2. To study the individual differences in subject response to drugs.

Methods Employed: During the past year we have altered the procedure employed in measuring the psychological effects of drugs such that instead of employing a number of separate pieces of apparatus we now use a single multiple stimulus-response apparatus. This allows the measurement of a variety of types of behavior involving the same motor response on the part of the subject. This multiple stimulus-response apparatus was developed by Michael Davis, formerly of Technical Development, with the collaboration of Dr. James Birren, Section on Aging, Laboratory of Psychology, and Conan Kornetsky, Laboratory of Clinical Science. Three measures of behavior have been used this past year: Simple motor response, choice reaction time, and a simple learning task.

One experiment has been completed this year and another is in progress. The completed experiment compared the effects of 800 and 1600 mg. of meprobamate, 60 and 120 mg. of phenobarbital, and 5 and 15 mg. of d-amphetamine.

The second experiment which is still in progress compared the effects of chlorpromazine, dextro-amphetamine, pentobarbital, benactyzine, and alcohol in normal subjects. The purpose of this experiment was primarily to test the hypothesis that individuals whose performance was most impaired by depressant drugs would have the greatest facilitation after stimulant drugs. In order to obtain facilitation after dextro-amphetamine this drug was administered after 48 to 72 hours of sleep deprivation.
In both of these studies Dr. Allen Mirsky of the Section on Animal Behavior, Laboratory of Psychology, determined the effects of the drugs on the "continuous performance test." (See Dr. Mirsky's report for details). Dr. Philippe Cardon of the Laboratory of Clinical Science studied the subjects employed in the first study. He compared the effects of the various drugs on a number of physiological indices. (See Dr. Cardon's report for details). Dr. Virgil Carlson of the Section on Perception and Learning, Laboratory of Psychology, has been testing all subjects of the second study on a suggestion test and a variety of perceptual tasks. (See Dr. Carlson's report for details). Dr. Isabelle Kendig of the Laboratory of Psychology has interviewed all subjects prior to the start of the experiment in an attempt to see if relationships exist between health and health attitudes and response to drugs. (See Dr. Kendig's report for details). Dr. Darab Dastur of the Section on Cerebral Metabolism, Laboratory of Clinical Science, has collected urine during the sleep deprivation part of the experiment to determine if sleep deprivation changes the constituents of the urine.

Major Findings: In the first study employing meprobamate, phenobarbital and dextro-amphetamine, only 1600 mgm. of meprobamate caused significant impairment of functioning on all three parameters of the multiple stimulus-response apparatus. Eight hundred mgm. of meprobamate reduced the rate of learning but did not affect performance on simple motor response or choice reaction time. Phenobarbital did not significantly affect performance on any of the procedures. Dextroamphetamine did not facilitate performance; on the contrary, it produced a slight though statistically insignificant impairment of performance.

In the second experiment, 14 subjects have been studied. The data will not be analyzed until 18 to 20 subjects have been completed.

Significance to Mental Health Research: This project will give information on the relative effects on performance in normal man of a variety of drugs that are used in the treatment of mental illness. In the early studies, it was found that those subjects who were most affected by one drug were very likely to be the same subjects who were most affected by other drugs. If this finding is confirmed, an attempt can be made to relate this to such variables as personality and the physiology of the individual. Such studies may give us a basic understanding of the important non-drug variables in an individual's response to drugs.

Proposed Course of the Project:

1. The present study will be completed early in 1958 after which further studies on individual differences in drug response will be carried out and the relationship of these responses to the response of the individual to psychological and physiological stress will be determined.

2. The effects of smaller doses of the drugs will be studied in an attempt to ascertain minimal effective dose.

Part B included: Yes.
Prt B.

Publications:


Honors: Dr. Conen Kornetsky was elected to membership in the American Society for Pharmacology and Experimental Therapeutics.
Project Title: Studies on the effects of various centrally acting drugs in the rat.

Principal Investigator: Conan Kornetsky, Ph.D. and Joseph Cochin, M.D.,

Other Investigators: Michael Malamud and Straty Economon

Cooperating Units: Laboratory of Chemistry, NIAMD

Man Years (calendar year 1957): Patient Days (calendar year 1957):
Total: 5/6 None
Professional 1/3
Other: 1/2

Project Description:

Objectives: 1. To study the effects of various centrally acting drugs on simple motor behavior in the rat.

2. To determine the degree to which individual differences in the extent of response to drugs may be partially independent of the drug being studied.

3. To study tolerance to various centrally acting drugs.

Methods Employed: The primary dependent variable used in these experiments is the time it takes the rat to swim a circular pathway 13 feet in length. Two experiments comparing the effects of chronic administration of morphine on swimming time to an analgesic measure of morphine effects have been completed. Two methods of determining analgesic effects have been used: tail flick response to thermal radiation and the hot plate method. A third and preliminary experiment has been started to study tolerance of the rat to LSD.

Major Findings: The morphine studies suggest that tolerance to the behavioral effects of morphine lasts longer than tolerance to the analgesic effects. The preliminary LSD experiments suggest that tolerance to LSD in the rat does not develop so rapidly or to so great a degree as does tolerance to LSD in man. Also, it is not clear at the present time whether or not complete tolerance to LSD ever appears in the rat.

Summer students
Significance to Mental Health Research:

1. These studies will help us understand the course of the development of tolerance to various drugs used in the treatment of the mentally ill.

2. A more basic problem but one that may have far more significance to the problems of mental disease is that of individual differences in response to drugs. If animals that are most affected by one drug are also the same animals that are most affected by other drugs, it will indicate that there is something present in the animal that determines the relative effects of drugs independent of the drug. If physiological mechanisms can be elucidated that contribute to the extent of drug effect it will contribute to an understanding of the important variables in human response to drugs.

Proposed Course of Project: The effects of a variety of drugs on the swimming procedure will be studied. If it is found that animals who are relatively most affected by one drug are relatively most affected by other drugs, an attempt will be made to elucidate the important variables contributing to individual responsivity to drugs.

Part B included: No
Project Title: A comparison of the effects of chlorpromazine and secobarbital on intellectual, motor and perceptual behavior in schizophrenic patients.

Principal Investigator: Conan Kornetsky, Ph.D.

Other Investigators: Ronald Wynne, M.S., Edward V. Evarts, M.D., and John M. Petit, M.D.

Cooperating Units: St. Elizabeths Hospital, Washington, D.C.

Man Years (calendar year 1957): Patient Days (calendar year 1957):
Total: 1 1/6
Professional: 1/2
Other: 2/5

Project Description:

Objectives: To compare the effects of both acute and chronic administration of chlorpromazine and secobarbital on a variety of behavioral measures in schizophrenic patients.

Methods Employed: Acute Study - Twelve schizophrenic patients with a minimum of one year of hospitalization were selected from the population of the William A. White Building at St. Elizabeths Hospital. On separate days each subject received 100 and 200 mgm. of secobarbital, 100 and 200 mgm. of chlorpromazine, and a placebo. Each dose of each drug was repeated once, so that each subject had a total of 10 testing days. All drugs were administered in identical capsules and the "double-blind" procedure was used throughout. Ninety minutes after drug administration, subjects were tested on a variety of motor, intellectual and perceptual tests.

Chronic Study - A week after the completion of the acute study, subjects were placed on a two-week regime of chlorpromazine, secobarbital, or placebo. All subjects received each drug for two weeks. A balanced design was used. During the first week on each drug, subjects received 100 mgm. twice a day, while during the second week subjects received 200 mgm. twice a day. Testing was done on the fifth day of each week. The same behavioral measures used in the acute study were used in the chronic study.
Major Findings: Acute Study - The results indicate that the effects of chlorpromazine and secobarbital on performance in schizophrenics are not significantly different from the effects of these drugs on performance in normal subjects. That is, both 200 mgm. of secobarbital and 200 mgm. of chlorpromazine impair intellectual, perceptual and motor functioning in both normal and schizophrenic populations. In the studies on normal subjects 100 mgm. of chlorpromazine also significantly affected performance on these same tests; in the schizophrenic population, however, 100 mgm. of chlorpromazine caused a slight but statistically insignificant decrement in performance level.

Chronic Study - In the chronic study neither 100 nor 200 mgm. of chlorpromazine caused significant impairment in performance, whereas the 200 mgm. dose of secobarbital did cause significant impairment of performance.

Research:
Significance to Mental Health/ Since drugs are one of the primary methods used in the treatment of the mentally ill, it is important to know to what degree these drugs do or do not impair psychological functioning. Drugs which lead to amelioration of a patient's psychotic symptoms but cause significant impairment of mental functions may not be the therapy of choice in certain groups of psychiatric patients.

Proposed Course of the Project: In 1958 this project will make use of operant conditioning procedures in the study of the effects of drugs in schizophrenic patients. It is hoped that the use of operant conditioning procedures will allow the studies of learning and perception in patients who otherwise would not cooperate enough so that meaningful results could be obtained. These techniques may prove useful in evaluating the efficacy of tranquilizing drugs in this population.

Part B included: No
Prt A.

Project Title: Behaviorally and pharmacologically induced effects on the electrical activity of the brain.

Principal Investigators: Edward V. Evarts, M.D. and Corwin Fleming, M.D.

Other Investigators: Mortimer Mishkin, M.D. and Bonnie Peacock

Cooperating Units: Section on Animal Behavior, Lab. of Psychology, NIMH

Man Years (calendar year 1957): Patient Days (calendar year 1957):
Total: 1 5/6
Professional: 5/6
Other: 1

Project Description:

Objectives: In the previous annual report (1956) from this section, two separate neurophysiological projects were outlined, one dealing with neuropharmacology and one dealing with the excitability of primary and diffuse thalamo-cortical projection systems. These two areas of investigation have been combined in the present project. The purpose of this project is to correlate a variety of behavioral and electrophysiological observations. Studies of the effects of pharmacological agents on behavioral and electrophysiological events are also in progress.

Methods Employed: Most of the studies on this project have been carried out in cats with chronically implanted electrodes. The loci of placement of the stimulating and recording electrodes depends upon the particular phase of neural activity under investigation.

Major Findings:

(1) Studies of the characteristics of cortical recruiting responses in unanesthetized cats were begun in 1955 in collaboration with Dr. H. W. Magoun. These studies have been completed. It was found that well-developed cortical recruiting responses could be evoked in awake cats by stimulation of the intralaminar nuclei. Stimulation of the brain stem reticular formation reduced the amplitude of the recruiting responses in these preparations; novel auditory stimuli had a similar effect. With repeated presentation, a given auditory stimulus ceased to affect recruiting responses ("habituation"). Repeated stimulation of the brain stem reticular formation, however, consistently reduced the amplitude of recruiting responses.
Previous studies carried out in collaboration with Dr. Arnold Schoolman and Dr. Wade H. Marshall demonstrated that pentobarbital has marked effects on the excitability cycle of the primary cortical response to lateral geniculate radiation stimulation. This effect of pentobarbital consists of a marked increase in the initial subnormality of the test response. Further studies have now shown that ethyl ether has a similar effect. In contrast, chlorpromazine and reserpine do not exert this depressant effect on the early phase of the cortical excitability cycle.

A series of observations concerning the electrophysiological effects of metabolites of epinephrine and norepinephrine has been carried out. In anesthetized cats, metanephrine and normetanephrine were tested on

(a) the transcallosal response
(b) the cortical response to retinal photic stimuli

In unanesthetized cats with chronically implanted electrodes, observations were made on the effects of the two substances on

(c) recruiting responses
(d) the cortical response to geniculate radiation stimulation
(e) the cortical response to retinal photic stimuli.

Large doses of the two substances were without effect on any of these forms of electrical activity.

Studies aimed at analysis of electrophysiological correlates of conditioning have recently been undertaken in collaboration with Dr. Mishkin. In an initial phase of this study, cats with chronically implanted electrodes were subjected to repeated photic stimuli. In three cats that were exposed to 3,000 flashes (600/day for 5 days), no decrease in the amplitude of the primary cortical response was observed. On the contrary, there was a statistically significant increase in the amplitude of the responses over this period. Subsequent studies will analyze the effects of a conditioning procedure in which the light flash will be paired with a painful shock.
Significance to Mental Health Research: The four general findings which have been described may be divided into two groups:

1. The electrophysiological studies have shown rapid habituation to the effect of an auditory stimulus on recruiting responses, but have failed to show any decrease in the primary cortical response to a repeatedly presented flash. These observations are related to the problem of central electrophysiological changes in association with learning, and may be regarded as generally relevant to basic problems of mental function.

2. The pharmacological studies have demonstrated a clear and striking difference between the cortical effects of barbiturates and ether on the one hand, and chlorpromazine and reserpine on the other. The absence of cortical depression by chlorpromazine and reserpine may in part explain the selective behavioral effects of these drugs.

Proposed Course of Project: The project will continue along the lines indicated above. During the coming year emphasis will be placed on studies of the electrophysiological correlates of learning and conditioning.
Part B.

Publications


NATIONAL INSTITUTE OF MENTAL HEALTH

Clinical Investigations
Laboratory of Clinical Science—Section on Psychiatry

BUDGET SHEET

Estimated Obligations for FY 1958

Total: $220,722

Direct: $83,673

Reimbursements: $137,049

Projects included: M-CS-Ps(C) 1 through M-CS-Ps(C) 5
Part A.

Project Title: Correlation of Psychiatric Evaluation with Neurophysiological, Psychological and Sociological Evaluation in the Aged.

Principal Investigators: Seymour Ferlin, M. D. and Robert N. Butler, M. D.

Other Investigators: None

Cooperating Units: Section on Cerebral Metabolism, Laboratory of Clinical Science, National Institute of Mental Health. Serial No. M-CS-CM-1

Man Years (calendar year 1957): 4.5
Patient Days (calendar year 1957): 753

Project Description:

Objectives: (a) To select suitable samples of "normal-aged" volunteers and Chronic Brain Syndrome patients for multidisciplinary study. (b) To psychiatrically evaluate and characterize the selected subjects in terms of: diagnosis, psychopathology and modes of adaptation. (c) To correlate psychiatric evaluation with physical status, neurophysiologic (including cerebral metabolism and electroencephalographic measurements) status, and psychological and sociological status. (d) To define (through a, b and c) criteria for the subgroups designated "normal" aged, "senile factor" aged, and chronic brain syndrome.

Methods: Each subject will be interviewed for two 2-hour recorded and observed sessions; the first (Interview A) being an unstructured psychiatric interview, the second (Interview B), a structured interview which includes a mental status examination and inquiry regarding apparent age-relevant concepts. There is systematic rotation in roles of interviewer and observer.

In addition, rating methods will be adapted for use by the interviewer, observer, and other psychiatrists for independent assessment.

Independent and consensus ratings, quantified on a seven-point scale wherever feasible, will be made in the following ten categories: (a) Diagnoses, (b) "Age Relevant" Symptoms,
Project Description: (Continued)

(c) Mental Status, (d) Affective State, (e) Psychiatric Symptoms, (f) Separation Response, (g) Concept Evaluation (Disordered Time Sense; Constriction of Future; Age Change Attitudes; Death Concern; Disturbed Body Image), (h) Maternal Attitude Scale, (i) Psychodynamic Formulation, and (j) Interview Behavior Scale.

Patient Material:

Major Findings: Adaptational modes in the aged have been derived from the psychiatric characterization and differentiation of emerging subgroups within the fifty-seven aged volunteers studied.

Investigations of neurophysiological variables; e.g., cerebral metabolism, in the community aged failed to disclose any simple relationships with psychiatric status (including cognitive defects). The relationship of reduced cerebral metabolism to the diagnosed of chronic brain syndrome was confirmed.

A group which has been designated as the "Senile Factor Group," reveals definitive cognitive losses but no alterations in cerebral metabolism. This may be a composite syndrome, a consequence of both organic and psychosocial alterations, and is distinct from the Chronic Brain Syndrome. This syndrome may correlate with psychological tests for "organicity." This may represent an early stage of the Chronic Brain Syndrome.

Investigations of the effects of psychosocial disruptions or losses demonstrates that the personal meaning or psychological significance, of such are more important than the incidence or nature of these stresses per se. In general, the adaptive or maladaptive function of personality variables or psychopathological features varied with the psychological significance of certain events in the aging experience (e.g., losses; cognitive deficits; forced retirement and the like).

The adaptive use of psychopathology, the use of activity, the counterphobic attitude, and the function of denial versus insight into the aging experience, are among the adaptational modes identified. On the other hand, maladaptation is seen in depression, paranoid isolation, identity loss and the like.

While the representativeness of the sample cannot be claimed a variety of psychiatric, psychosocial and other aspects of these populations are explicitly characterized and thus available for purposes of comparison.

Significance to Mental Health Research: The structuring of problems for research in geriatric psychiatry receives much of its impetus in the context of the ever-increasing numbers of aged in this country. The older person himself has been neglected research-wise and there has been much faulty extrapolation of data from other ag
Significance to Mental Health Research: (Continued)

periods. The study of the normal aged has been especially neglected. The search for adequate evaluation in the aged has its historic roots in the inability to fully understand psychological symptoms on the basis of neuropathological changes. The question as to which are the important parameters for investigation emphasizes the need for a multidiscipline approach. Psychiatric diagnoses run the gamut and may vary from one dealing with the individual’s personality make-up to defined neurotic symptomatology to organicity; e.g., chronic brain syndrome with arteriosclerosis. Thus the possibility of correlating data with other disciplines is present. A few examples of the theoretical questions posed by one discipline against the data provided by another discipline are as follows: (1) Does the slowing of reaction time postulated by the psychologist as a sine qua non of aging correlate selectively with depression as evaluated by the psychiatrist? (2) Does the diagnosis of chronic brain syndrome with arteriosclerosis formulated as a syndrome by the psychiatrist correlate with evidence of change as measured by the neurophysiologist and internist? (3) Are assumptions regarding sequence of changes in cerebral blood flow and metabolism as measured by the neurophysiologist supported by changes in intelligence, perception, etc., as measured by the psychologist and psychiatrist? Follow-up studies, if undertaken, can deal with the predictive value of such material.

Proposed Course of Project: The study of the subgroup of hospitalized Chronic Brain Syndrome patients will be continued.
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:


Perlin, S., Pollin, W. and Butler, R. The Experimental Subject: I. The Psychiatric Evaluation and Selection of a Volunteer Population. (Submitted for publication)

Honors and Awards relating to this project:

Part A.

Project Title: Psychiatric Evaluation of Normal Control Volunteers.

Principal Investigators: William Pollin, M. D., and Seymour Perlin, M.D.

Other Investigators: None

Cooperating Units: None

Man Years (Calendar year 1957): Patient Days (Calendar year 1957):
Total: 1.20
Professional: .50
Other: .70
85

Project Description:

Objectives: (a) To study the methodology of evaluating normal control volunteers. (b) By means of psychiatric evaluation, to describe the psychodynamics of all normal control volunteers admitted to the Laboratory of Clinical Science for participation in other projects. (c) To provide data for use in (1) setting up criteria for selection of normal control volunteers; and (2) interpretation of the results of projects in which they participate. (d) To indicate in what ways extension of this investigation into the area of correlation between psychological and physiological variables in normal controls can be made. (e) To study the motivation of normal control volunteers to enter a research hospital and the relationship between motivation and psychopathology.

Methods Employed: Each normal control is routinely seen for a psychiatric evaluation interview. Following this interview, the interviewer as well as the interviewee provide independent ratings of a variety of categories of affect and psychological functioning, quantified on a 7-point scale. In addition, interview behavior is rated by the psychiatrist. Interviews are recorded and available for later independent analysis and evaluation. During their stay on the ward, subjects are seen before and after certain investigative procedures for brief, recorded procedure-oriented interviews.

Patient Material: To date, (10/17/57) 49 subjects have been so evaluated.

Major Findings:
1. Psychiatric evaluation of a group of 29 volunteer research subjects demonstrated the presence of significant psychopathology in 15. In 11 of the 29 subjects psychiatric diagnoses were made.
Major Findings:

2. There was an inverse relationship in this volunteer group between the presence of psychopathology and the extent to which environmental influences contributed to serving as a volunteer.

3. The incidence of psychopathology in a subgroup whose volunteer status was largely due to their draft status was 26%; in a second subgroup whose volunteer status conformed with sociocultural tradition, 59%; in a third subgroup where neither of these factors were operative, 100%.

4. The volunteer group showed considerable differences in the motivations involved in volunteering, in the ability of its members to accommodate to stress, in defense mechanisms employed, and in the tendency to somatize anxiety.

5. These differences, and the relationship between volunteering and psychopathology have clarified a number of questions pertinent to the selection of volunteer groups, and the interpretation of results obtained from them.

Significance to Mental Health Research: Normal control volunteers constitute one of the major subject groups used in psychiatric and psychological research. Until very recently, little attention has been given to setting up criteria for the selection of such groups, other than attempts at exclusion of individuals showing gross psychopathology. Similarly, there has been little work done on psychiatric evaluation of normal controls or with the application of data obtained from such evaluation to the interpretation of data obtained by other disciplines. Findings thus far make possible a more meaningful use of volunteers, and clarify some problems of one of the basic elements in personality and psychophysiological research: the subjects employed.

Proposed Course of Project: Evaluation of all normal control volunteers admitted to the Laboratory of Clinical Science wards will continue.
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:


Honors and Awards relating to this project:

Part A.

Project Title: Psychological Variables and Cerebral Physiology.

Principal Investigators: Seymour Perlin, M. D. and William Pollin, M. D.

Other Investigators: Conan Kornetsky, M. D., Louis Sokoloff, M. D., and Seymour S. Kety, M. D.

Cooperating Units: None

Man Years (calendar year 1957): Professional: .66
Patient Days (calendar year 1957): Other: .33

Total: .33

Project Description:

Objectives: To determine whether there is a demonstrable relationship between levels of cerebral blood flow and/or oxygen uptake, on the one hand and basic personality structure and/or psychological state at time of the procedure, on the other. To characterize such a relationship, if one exists.

Methods Employed: Normal Control Volunteer subjects are routinely seen for psychiatric evaluation on admission. They are also seen at intervals before and after the CBF procedure, by the psychiatrist, for a brief procedure-oriented interview. Psychological measurements, including MMPI, Rorschach and GSR recording during procedure, are done. Cerebral blood flow and metabolism are measured by Nitrous Oxide technique of Kety and Schmidt. Four participant-observers make independent and consensus ratings of subjects behavior and adaptation during procedure. When current second series of subjects is completed, these independently amassed data will be inspected for possible correlations and to determine if certain relationships between personality and cerebral metabolism indicated by the study of first series of subject is further supported.

Patient Material: Males - 5 x 2 - 10
Females - 6 x 2 - 12
Patients served on a variety of projects

Major Findings: In the first group of subjects, studied by similar techniques, there appeared to be an inverse relationship between low normal levels of cerebral O₂ uptake and the presence of psychopathology. There was also a direct relationship between level of CMRO₂ and responsivity during the procedure. The current subject population is being investigated to determine if these previous findings can be verified.
Patient Material:

Males - 5 x 2 - 10  Patients served on a
Females - 6 x 2 - 12  variety of projects

Significance to Mental Health Research: Results of this study should help to clarify the relationship between personality factors, the stress of certain investigative procedures and the results of such procedures. They may also indicate a relationship between certain aspects of cerebral metabolism and personality variables.

Proposed Course of Project: The present second series of subjects will be completed and data then analyzed.

Part B included  Yes
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:

Honors and Awards relating to this project:

Presented at (1) Peripatetic Club, February 1, 1957; and (2) Public Health Service Clinical Society, April 27, 1957; under title "Psychological Variables and Cerebral Functions in a Volunteer Population: Preliminary Report."
Part A.

Project Title: Correlation of Psychiatric Evaluations and Their Physiological Correlates of the Effects of 1-Epinephrine in a Normal Control and A Schizophrenic Population.

Principal Investigators: Robert N. Butler, M. D. and William Pollin, M. D.

Other Investigators: None

Cooperating Units: Section on Cerebral Metabolism Section, General Physiology

Man Years (calendar year 1957): Patient Days (calendar year 1957):
Total: .10 None
Professional: .50
Other: .60

Project Description:

Objectives: (1) To determine if there is any difference in psychiatric response to a high level of circulating epinephrine between a group of chronic schizophrenics and a group of control volunteers. (2) To study the effects of a high level of circulating epinephrine upon the schizophrenic disorder. (3) To investigate possible correlations between psychiatric response to high levels of epinephrine and concurrently obtained metabolic and psychophysiological data.

Methods: Each experimental subject receives 1-Epinephrine, standardized according to body weight, infused intravenously at 0.30 micrograms per kilogram per minute. An aliquot of tagged tritiated epinephrine is included in the infusion. Experimental conditions are standardized and studies of control and schizophrenic subjects are interdigitated. Two psychiatrists participate, one as an interviewer and the other as an observer-auditor. The psychiatric observations proceed continuously from the time the patient is informed of the procedure shortly before it begins through a post-study evaluation period. The procedural period consists of a randomized sequence of drug and saline infusion concerning which the participating psychiatrists remain blind. The subject also is uninformed as to what substance is being infused. During each infusion period an interview of approximately twenty minutes duration is conducted. The interview includes a portion of the time devoted to unstructured productions by the subject, a standardized symptom check list, brief tests of mental function, and, in the case of the
schizophrenic population, specific questions pointed at each subject's most prominent psychotic features of conflict. The interviews will be recorded for further and independent analysis.

The observer-auditor employs a scale devised for use in rating subjects with respect to changes in affect, mental organization and activity in each of the periods, and in assessing their attitude toward the procedure. In addition, he writes continuous descriptive notes and includes data concerning the interaction between the interviewer and the subject. Observations are made through a one-way mirror.

Physiological, metabolic, psychophysiological and EEG data are collected simultaneously.

**Patient Material:** A group of chronic schizophrenic patients admitted here from a state hospital, as well as a group of resident control volunteers.

**Significance to Mental Health Research:** The role of epinephrine in anxiety has been suspected for some time and the possibility that epinephrine or one of its metabolites is of importance in the pathogenesis of schizophrenia is under current consideration. Studies of the psychological and physiological effects of epinephrine may contribute to knowledge of the physiology of affects and/or the physiology of schizophrenia.

**Proposed Course:** Trial studies are now being conducted on both control and schizophrenic subjects. The series itself will shortly begin.
Part A.

Project Title: Psychiatric Investigations in the Biological Study of Schizophrenic Subjects.

Principal Investigator: Seymour Perlin, M. D.


Cooperating Units:

Man Years (calendar year 1957): Patient Days (calendar year 1957):
Total: 1.2 735
Professional: 2.5
Other: 3.7


Objectives:
(1) a. To critically explore schizophrenic subject selection criteria compatible with the theoretical and methodological approach of the multidisciplinary team. b. To present a design for selection, which attempts to increase the probability of the expression (qualitative and/or quantitative) of a biological defect. c. To detail the application of the design in a current NIMH project.
(2) To characterize, in detail, relevant personality features and adaptations of a normal control and a schizophrenic population admitted for psychophysiological studies in schizophrenia. To this end, to develop interview techniques, and rating scales, which will be applicable to both groups. Within the schizophrenic group, to determine if there exist certain patterns of disease, or symptom clusters, which, though possibly independent of currently accepted diagnostic groupings, show significant correlations with organic groupings.
(3) a. To observe the behavior of schizophrenic subjects in a research setting for correlation with psychiatric interview predictions and psychological test findings. b. To characterize the experimental situation, and investigate the perception and response of control and schizophrenic subjects to the experimental situation. This is an attempt to control for situational variables extrinsic to the schizophrenic disorder.
(4) The overall objective is to develop a psychiatric ward milieu suited to the requirements of biological studies. Complicated by this goal, but in many ways crucial to its achievement, is the more limited objective of providing a desirable standard of psychiatric care for the patients participating in such studies.

Methods:
(1) In attempting to establish criteria compatible with the theoretical and methodological approach of the multidisciplinary team, the following issues were delineated: (A) Group homogeneity; e.g., age, sex, duration of hospitalization, exclusion of known organic factors. (B) The biasing of the sample: An attempt to increase the probability of the expression (qualitative and/or quantitative) of a biological defect. Concepts utilized: Multiple versus single etiology, "genetic," familial, "process," etc. (C) Generalizations and statistics related to the small sample. (D) The "normal control."

The following committee was consulted as regards the issues raised: Dr. Seymour Kety (Biology); Dr. Gordon Allen (Genetics); Dr. Samuel Greenhouse (Statistics).
(2) Clinical experience and literature search have provided a number of alternative interview- and rating scale approaches, which are currently being tested.
(3) Observation by ward personnel and the investigator. Use of several scales devised to record and quantify particularly changes in affect, mental organization and activity observed in the ward and in the experimental situation.
(4) In the process of administering the ward there are many unusual problems related to the research goals. Through such pragmatic and empirical experience ward policies, modes of interaction with patients, and distinguishing characteristics of the ward milieu are gradually being shaped and defined.

Patient Material:
Major Findings: None

Significance to Mental Health Research: The selection, evaluation and ward observations of schizophrenic subjects are essential aspects of biological studies in schizophrenia. (Such factors are, in themselves, areas for research.)

Proposed course: At present, plans call for the admission of 14 schizophrenic subjects and 14 "normal control" volunteers for long-term biological studies.

Part B included No
Basic Research
Laboratory of Neurophysiology
General Neurophysiology

BUDGET SHEET

Estimated Obligations for FY 1958

Total: $140,400
Direct: $107,876
Reimbursements: $32,524

Projects included: M-NP-GN 1 through M-NP-GN 8
Part A.

Project Title: Measurement of Local Circulation in the Brain

Principal Investigator: D. Hansen

Other Investigators: L. Sokoloff and W. Freygang

Cooperating Units: Laboratory of Clinical Science, Section on Cerebral Metabolism, M-CS-CM-3

Man Years:
  Total: .5
  Professional: .5
  Other:

Project Description: See M-CS-CM-3
Part A.

Project Title: Effects of drugs on specific ionic conductance.

Principal Investigator: W. H. Freygang, Jr.

Other Investigator: None

Cooperating Units: This work is being done with Dr. A. M. Shanes of the Institute of Arthritis and Metabolic Diseases and Dr. H. Grundfest of the Department of Neurology, Columbia University, New York

Man Years: Total: .15
            Professional: .15
            Other:

Project Description:

Objectives: It is possible to analyze the components of membrane permeability into those which are specific for different ion species. A new understanding of the mechanism of the nerve impulse has been achieved with this approach. The effects of many neurologically potent drugs need to be studied in the light of this new information in order to define clearly their mode of action.

Methods Employed: The technique employed provides a controlled voltage across the membrane of a squid giant axon. Changes in the flow of ionic current across the membrane have been measured. The drugs are applied extra-cellularly. Cocaine and veratrine have been studied.

Major Findings: A prominent effect of cocaine is a reduction in the influx of sodium ions during activity of the axon.

Significance to Mental Health Research: The study should supply information of fundamental neuropharmacological importance.

Proposed Course of Project: Analysis of data.

Part B included Yes ___ No x
Part A.

Project Title: Measurement of Soma-Dendritic Membrane Current.

Principal Investigator: W. H. Freygang, Jr.

Other Investigator: H. Wiener

Cooperating Units: None.

Man Years:
  Total: 1.80
  Professional: .80
  Other: 1.00

Patient Days: None.

Project Description:

Objectives: To determine the role of the dendrites and cell bodies in the process of transmitting electrically coded information in the central nervous system.

Methods Employed: As the dendrites and cell bodies carry signals, there is a flow of current across their membranes. It has been proven both by mathematical means and by an electrical analogue of a neuron that the electric potential outside the cell, but very close to it, is directly related to the flow of membrane current. The extracellular potentials are recorded from very fine glass pipettes placed close to a single neuron and the time course of the membrane current is calculated from the recordings.

Major Findings: It is apparent that the intracellular recording technique does not show whether the site of recording can produce all-or-none electrically induced activity or not, for the electrical signs of all-or-none activity can spread in a relatively undistorted form to the recording site. The time course of the membrane current from the dendrites and cell bodies, however, shows that these parts of the neuron do not respond to electrical excitation. Therefore, they must be activated primarily by chemical transmitter substances that do not induce all-or-none propagating electrical activity.

Significance to Mental Health Research: This new technical approach combined with the finding that the dendrites and cell bodies are not excited electrically makes it possible to investigate the chemically excitable soma-dendritic membrane...
Part A. (continued)

with a clearer understanding and possibly a powerful new tool.

Proposed Course of Project: Because the anterior horn cells of
the spinal cord are large and can be impaled easily, much intra-
cellular data have been obtained from them. Also, they have the
additional advantage that they respond synaptically to stimula-
tion of several easily accessible pathways. For these reasons
it seems probable that the nature of synaptic excitation can be
studied more profitably with these nerve cells rather than those
of the lateral geniculate nucleus which have been studied in
this project.

Part B included       Yes  x  No  ___
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:


Honors and Awards relating to this project:

None.
Project Title: Studies on Role of Superficial Neurons "Dendritic Reactions" in Spreading Cortical Depression.

Principal Investigator: Wade H. Marshall

Other Investigators: W. H. Freygang, Jr.

Cooperating Units: None.

Man Years
Total: .90
Professional: .30
Other: .60

Project Description:

Objectives: To determine relation of reactivity of superficial elements of cortex to spreading cortical depression in cat and monkey. The reactivity of superficial elements is typically recorded electrically as a surface negative wave. This reaction has been rather loosely designated as the dendritic response. Spreading cortical depression can be obtained in cat and monkey only by pathological manipulation, that is by prolonged exposure to room air, cooling the surface of the cortex, treating the surface with Tyrodes containing excess potassium, etc. The latter two methods have been extensively employed in this laboratory. The effect of these manipulations on the "dendritic" response was determined.

Methods Employed: The "dendritic" reaction was evoked by direct stimulation and by stimulation of the callosal system. The surface of the arachnoid membrane was exposed to excess potassium or cooled to the level at which spreading depression can be evoked.

Major Findings: It was found that producing conditions under which spreading depression can be evoked resulted in severe reduction in the "dendritic" response. This reaction is reversible. These experiments clearly showed that neuron activity of, at least, the first layer of the cortex is not necessary for evocation and propagation of spreading depression. This is a curious result since it is known that the upper third of the cortex is dominant in the spreading depression reaction.
Part A. (continued)

Conversely, the rabbit and other smooth brain corticies are very susceptible to spreading depression and it occurs in these cases with no specific pathological manipulation and with the "dendritic" response intact.

Significance to Mental Health Research: Further progress in fundamental physiology of the brain.

Proposed Course of Project: Various aspects will be continued indefinitely.

Part B Included: Yes___ No x
Part A.

Project Title: Effect of Curare on the "Dendritic" Reaction

Principal Investigator: Wade H. Marshall

Other Investigators: J. Brinley, E. Kandel, S. Lerner, T. Bak

Cooperating Units: None

Man Years:
Total: 1.70
Professional: .60
Other: 1.10

Project Description:

Objectives: To test the published claim that large doses of curare transiently block the synaptic reactions allegedly involved in the "dendritic" reaction.

Methods Employed: It was soon found that the great fall in systemic blood pressure resulting from injections of large doses of curare (3 to 10 mg/K) led to various artifacts, depending on type of electrodes employed and methods of suspending same. With spring-loaded electrodes the fall of capillary pressure may result in collapse of the capillary wall under pressure of the electrode, this being followed by reduction or extinction of the reaction. With fixed electrodes the brain shrinks away from them as the blood pressure falls resulting in less effective stimulation and recording, thus giving the appearance of a reduction of response. In any case with spring loaded or fixed electrodes spreading cortical depression often occurred after the injection of curare. Hence we developed a new method of stimulation and recording which eliminates the above and other artifacts from the direct cortical response (dendritic) and callosal reactions. This consisted essentially of a system of reversible pore electrodes mounted in a constant pressure device, the pressure being enough to secure good contact without collapsing capillaries even at very low systemic blood pressure. This system also permitted the
Part A. (continued)

electrodes to follow the surface as the brain volume increased or decreased. This technique is absolutely essential for reliable results in those kinds of experiments.

Major Findings: We found that large doses of curare do not block the direct cortical (dendritic) response when the above artifacts including spreading cortical depression are eliminated.

Significance to Mental Health Research: This new technical approach is a useful advance in techniques for experimentation on the brain. It is currently of some value to determine validity of the claim that curare blocks synaptic conduction in dendritic systems of the cortex.

Proposed Course of Project: Project Concluded

Part B Included Yes_x_ No_____
Part B. Honors, Awards, and Publications

Publications other than abstracts from this project:

Proponents of the above argument have been notified of our results. We may eventually publish this but since it is a negative result we wish to give the other laboratory time to recheck their findings.

Honors and Awards relating to this project:

Lecture at University of Washington Medical School and University of Wisconsin Medical School dealing with these kinds of experimental problems.
Project Title: Tests of Certain Drugs on Specific Electrical Reactions in the Brains of Animals

Principal Investigator: Wade H. Marshall

Other Investigators: E. Evarts, E. Kandel, J. Brinley, and S. Lerner

Cooperating Units: Laboratory of Clinical Sciences
Laboratory of Clinical Biochemistry
Heart Institute

Man Years
Total: .90
Professional: .40
Other: .50

Patient Days: None

Project Description:

Objectives: To further analyze neuron activity with the aid of specific drugs which may have specific roles in synaptic transmission, including those which are currently alleged to be demonstrable.

Methods Employed: Precise electrical technics are employed to test effects of drugs on the direct cortical and callosal reactions (the "dendritic" reactions), and on other systems such as the specific sensory, recruiting and augmenting reactions.

Major Findings: We have failed to see any specific action of adrenalin or serotonin when injected I.V. or in the carotid artery in the cat or monkey. Gamma amino butyric acid applied topically on the surface of the arachnoid membrane very quickly (order of 1 sec.) produces a dramatic reversal of phase of the surface negative "dendritic" reaction. Isotonic KCl similarly applied produces a sufficiently similar reversal so we currently conclude that the drug blocks the superficial elements unmasking surface positive recorded elements from slightly deeper structures. Quanido butyric acid topically applied seems to act oppositely to gamma amino butyric. It enhances the "dendritic" reactions.

Significance to Mental Health Research: Contributes to knowledge of physiology of the brain.

Proposed Course of Project: Continue indefinitely.

Part B Included: Yes   No
Part A.

Project Title: Activity Cycles and Interaction Between Callosal and Direct Cortical Reactions, and to Determine Regions of Chief Activity of Each.

Principal Investigator: Wade H. Marshall

Other Investigators: E. Kandel, J. Brinley, S. Lerner

Cooperating Units: None

Man Years:
- Total: 1.50
- Professional: .50
- Other: 1.00

Project Description:

Objectives: To get better data on interaction and activity cycles in the callosal, direct cortical response and other systems.

Methods Employed: Cats, monkeys and rabbits are used employing techniques developed in the course of the curare experiments and described in Project No. M-NP-GN-5.

Major Findings: This work is now in progress, no major findings to report at this time.

Significance to Mental Health Research: None

Proposed Course of Project: Continued indefinitely.

Part B. Included Yes_____ No X
Part A.

Project Title: Measurement of pH Changes in the Cortex During Spreading Cortical Depression

Principal Investigator: Wade H. Marshall

Other Investigators: J. Brinley, S. Lerner, T. Bak

Cooperating Units: Department of Physiology, University of California, Los Angeles. National Heart Institute, Laboratory of Technical Development

Man Years:
  Total: 1.20
  Professional: .20
  Other: 1.00

Project Description:

Objectives: To determine if a specific type of glass pH electrode could be used to estimate changes in pH during a wave of spreading cortical depression as has been reported by a laboratory at University of California, Los Angeles.

Methods Employed: Using electrodes kindly supplied by Dr. Ralph Sonnenschein, University of California, Los Angeles. We repeated their experiments with our methods of recording spreading cortical depression.

Major Findings: We found the Los Angeles laboratory to be in error, the difficulty lies in a very subtle and easily made error of interpreting the "D.C." shift accompanying spreading cortical depression.

Significance to Mental Health Research: Improved techniques for experiments on the brain.

Proposed Course of Project: Will continue with other and similar types of electrodes in collaboration with Dr. Murray Eden of the National Heart Institute.

Part B. Included Yes X No
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:

Since this finding is negative, it will not be published at present. The Los Angeles laboratory has been informed of our decision.
Basic Research
Laboratory of Neurophysiology
Section on Cortical Integration

BUDGET SHEET

Estimated Obligations for FY 1958

Total: $68,893
Direct: $52,933
Reimbursements: $15,960

Projects included: M-NP-CI 1 and M-NP-CI 2
Part A.

Project Title: Analysis of the Electrical Activity of the Brain of Unanesthetized Monkeys.

Principal Investigator: John C. Lilly

Other Investigators: Robert R. Cox

Cooperating Units: Swarthmore College and National Science Foundation

Man Years
Total: 1.08 1/3
Professional: .33 1/3
Other: .75

Project Description:
Objectives: 1. Analyze origins, courses, and relations of figures in the electrical activity in the brain of unanesthetized monkeys.
2. To correlate this activity with behavior and physiological and psychological states.
3. To analyze the electrical activity which occurs concurrently with locally stimulated "reward" and "punishment" systems within the brain itself.

Methods Employed: 1. Using implanted electrodes of a new design (see Project #2) it is intended to pick up the electrical activity from 256 points simultaneously within the substance of the brain of the unanesthetized monkey and relate this to the activities of the monkey. Development of a system for recording from 256 electrodes simultaneously was initiated 4 years ago with the electrical engineering department of Swarthmore College. Two National Science Foundation grants supported the two-year development which was completed last summer. It has been found this year that the prototype which was developed under these auspices is not quite simple enough in terms of ease of control to be immediately useful in long term studies. These circuits are being currently revised, a new type of simplified electronic switch has been developed recently. An 18-channel tape recorder was developed, delivered, and modified to record the switched outputs of 16 times 16 input channels.
Part A. (continued)

Major Findings: 1. Technical: the problem of electronic switches at low level has been continued to be attacked on this project. It is extremely difficult to obtain a switch which will operate rapidly enough and quietly enough in the electrical sense to give us the necessary information from the brain. Several forms of switches have been developed, tested and found to be inadequate. Currently a new model has been produced in a 25-channel prototype to be tested on animals.

2. Physiological: no physiological results have been obtained on this project during the last year. Previous work on the project with a 25-channel instrument showed that the electrical activity of the brain contains "figures" which start moving and die away in characteristic fashions which vary with states of excitement, drowsing, and sleep, with evoked responses, voluntary movements and epileptic seizures. These results have shown that 25-channels are not numerous enough and that the old recording system was not fast enough to adequately record the type of figures which occur when the animal is awake. These figures are very small and extremely rapid; the new 25-channel switch is presumably fast enough, combined with the tape recorder, to record and later reproduce these figures in a slowed down fashion.

Significance to Mental Health Research: Since the activity of the brain is the basis of all thought, emotion, and action it is necessary to investigate and understand this activity in as many ways as possible. Electrical methods have the advantage of high speed and local specificity, i.e. are closest to the very rapid action to the nerve cell groups themselves. Since the brain is a three dimensional, extremely complex, inter-related network of such groups of nerve cells it is necessary to observe simultaneously many loci at once in order to appreciate how this extremely complex "computor" operates. Since this is basic exploratory work it is hard to say what its significance will be in the future. These new methods are the first ones with a great enough ability to begin to record the large amounts of information needed to understand the complexities of the brain's action.

Proposed Course of Project: To further develop and use the 25-channel prototype of the 256-channel instrument and then to further develop the 256-channel instrument which is progressing simultaneously.

Part B included Yes [ ] No [x]
Project Title: Mapping the Behavior Elicitable by Electrical Stimulation of the Brain.

Principal Investigator: John C. Lilly.

Other Investigators: Alice M. Miller, Robert R. Cox, Horace W. Magoun, Felix Strumwasser.

Cooperating Units: Marineland Research Laboratory, Marineland, Florida

Man Years: 2.57 1/3

Professional: .57 1/3

Other: 2.00

Project Description:

Objectives: 1. Define and investigate those regions of the monkey brain which are of importance in terms of eliciting (1) specific somatic movements, (2) extreme emotional states, and (3) those which function as powerful motivational substrates: (a) various types of pleasure including sexual activities, (b) various types of punishment including pain, fear, etc. These studies are an extension of the previous work by Hess; Ranson and Magoun; Magoun and co-workers; Jasper; Olds and Milner; Delgado, Roberts and Miller; etc.

2. To continue development of the technical methods necessary to explore such things in the brain, safely and with relatively minimal injury due to mechanical insertion of electrodes and to the passage of electrical currents through the brain.

3. To investigate these systems in larger brained animals than the monkey such as the chimpanzee and the porpoise. The porpoise is an animal of choice because it is available through the Marineland Research Laboratories in Marineland, Florida; its brain is equal to and larger than the human and it has been demonstrated recently by Rose and Kruger that it contains, in an enlarged fashion, all of those nuclei which are considered to be characteristic of the human.

Methods Employed: 1. A simplified method of implantation of electrodes and electrode arrays into the brain through the skull and skin of unanesthetized monkeys has been developed on this
project within the last year. This method consists of hammering small guides into the skull in the stereotaxic instrument. Later these guides can be located through the intact skin and the electrodes inserted at will in a monkey or other animal. Such guides have been completed and inserted and used in monkeys and another type has been inserted and used in porpoises.

2. Records are taken of observations on the behavior during stimulation.

3. Operant testing methods. (B. F. Skinner) by "animal start" and "animal stop" stimulation methods of all areas stimulated in order to find (a) those areas which function as "animal start" areas, in other words, reward, i.e. pleasure and compulsive activity and (b) those areas which function as "animal stop" areas, i.e., punishment areas.

4. Testing interactions between the stimulation and other ongoing behavior such as eating, spontaneous muscular activity, naturally evoked emotional states, interactions with the observers, etc.

Major Findings: 1. Our confirmation of the finding of Schäfer von Bechterew, Ferrier, Sanderson, etc. continues, i.e. that every small area of the unanesthetized macaque cerebral cortex can cause a specific movement of relatively small groups of muscles and hence all of cortex is sensorimotor. (It was learned this year that Schäfer, in eliciting the post central motor map, was not using anesthesia contrary to implications in the published account.)

2. A system in the brain has been found which causes a clinical state which resembles "fright", extreme anxiety, or terror; it has been demonstrated that this state is unpleasant to the animal by showing that he can be taught to act to stop the stimulation and that once learned the reaction to stop the stimulus is not lost or forgotten as easily as that to stop a peripheral pain stimulus. This observation has been borne out in several animals who have been trained to avoid stimulation in this system at very low levels of current. If the animal is prevented from shutting the current off and it is allowed to rise to higher values, it is found that a high-priority, urgent escape pattern takes place in which the animal cannot function in the learned pattern but is forced to function in a violent multiple escape set of actions and shows extreme defensive reactions if any threatening object is brought near him. During this state vocalization seems to
be impossible; further back in the pain systems vocalization is easily elicitable and is part of the pattern of responses to pain, both centrally and peripherally. This observation has been suggestively borne out by work on humans by Wilhelm Sem-Jacobsen in Oslo, though his localization is not so good as ours; i.e. he has not been able to recover the brain. From his x-rays of the position of his electrodes in the midplane in relation to the base of the skull it is presumed that he was in the same system. The patient reports extreme terror which he cannot control and which does not have any of the aspects of a quasi-emotion or pseudoadjective state or sham fright that one might expect from results using epinephrine and norepinephrine. This system apparently does excite a primary emotion rather than merely the outward expression of such an emotion.

3. Continuation of the work on reward systems (Olds and Milner). We have mapped these systems in several monkeys. Stimulated in these zones an animal acts so as to start an electrical stimulus in his own brain. We have continued Olds' demonstrations that this kind of system operates as a powerful motive to learning new and difficult tasks, we have found that once the animal is taught this reaction, the learned pattern can be shifted from one output to another quite easily by the animal. He performs 3 times per second by hand, 2 per second by tongue, and 1 per second by foot; however, he very much prefers to use the hand. We have continued to try to force the monkey to vocalize to obtain this reward and find that it is not as powerful as the other outputs, in fact it requires a combined social situation plus the electrical stimulation so far; we are not sure we will not find some area which will give vocalization as an adequate output.

4. In two animals we have found a system which causes erection of the penis. This seems to be an additional part of a system recently described by MacLean. We have found that erection of the penis can be caused by stimulation of parts of the fornix and of the septal nuclei by electrical stimuli. MacLean demonstrated that erection can be aroused by chemical stimulation of the hippocampus from which the fornix originates. This system is unique in our experience in that it is both positively and negatively reinforcing, not simultaneously but sequentially in time. The animal will push a lever to start his own erections about once per minute and will stay awake 24 hours a day to continue this kind of activity. On the other hand, if we start the stimulus every 30 seconds he will shut off approximately
Part A. (continued)

every other one and will allow them to come through about once per minute.
5. Another very small system is being investigated in which the animal appears to have its "battery drained" when stimulated in this region. All of his spontaneous activity decreases, he becomes relatively unresponsive through not comatose or unconscious and if allowed to be alone will go to sleep, this apparently is very closely related to Hess' so-called "sleep area".
6. Technical Development: a new method of implanting electrodes which consists of hammering guides into the skull has very much simplified these problems. In the older system we implanted buttons in the skull which allowed up to 44 electrodes to be moved in and out of the brain, mapping up to 30-40 points along each electrode track; it was found that the skin broke down around such buttons after several months of use. In the new system each electrode penetrates the skin independently; intact skin is left between electrode So far there is some reaction at the point at which the electrode penetrates the skin but it is not nearly so severe as it was around the button. We now can map about 30-40 points along each electrode track from the top of the brain to the base of the skull in a much simpler fashion and yet be able to restore the animal to a colony or his cage without any leads showing from the top of the head. This system has also been developed for use on the porpoise; it was demonstrated 2 years ago that it is practically impossible to anesthetize the porpoise without using a respirator. With the new technique local anesthesia is introduced into the head to the skin down to the bone and the guide pounded in with porpoise suspended in the restraint system in water. The pain was sufficiently small so that the porpoise showed very little if any reaction to this procedure; he gave a small startle response at the first hammering apparently due to the sound and the sense of pressure but after that he calmed down and allowed us to keep on going without much trouble.
7. We have found that in two porpoises that (a) the reward and punishment systems exist and (b) that the urgency of these systems for the porpoise is comparable to that for the monkey, (c) that the porpoise learns very much more rapidly than the monkey to either turn the stimulus on or to turn the stimulus off, (d) that the porpoise in contrast to the monkey learns very rapidly with an assist from the observer on the proper way to push the trigger, and (e) that during
stimulation of a reward system in the porpoise he becomes extremely loquacious and covers a vast repertory of sounds apparently seeking some way of communicating with the observer in the fashion in which the porpoise will communicate with his own species.

Significance to Mental Health Research: These various regions of the brain which are so fundamental to behavior and the subjective life, are of fundamental importance to an understanding of those factors which maintain mental health and maintain mental illness. Studies upon the rat brain by Olds and Milner, on the cat brain by Hess, Delgado, Roberts and Miller, and Ranson and Magoun have finally given us powerful tools for the investigation of that which is urgent and of highest priority when active within the brain substance. These rewards and punishments and emotional elicitations are more powerful than any other way which we and others have been able to employ to change the behavior of animals; apparently these methods and these states exert more powerful effects than food, pain, and sex itself. Means have now been found for quickly inducing and as quickly removing profound mental changes in monkeys and in porpoises. In the rat, cat, monkey (chimpanzee), human, porpoise series, we have a spectrum of brain sizes in which we might expect there to be a spectrum of physiological determinants of behavior which can be elicited by small areas of intense activity elicited by electrical stimulation; it is important to investigate brains larger than the human before approaching the human in order to find out if the urgency and priority of these built-in emotional patterns exists in the larger brain and whether the larger brain can exert control over such patterns. Such methods ultimately should be applied to the human and currently are by several investigators. These show that the expected urgency of both the reward and punishment systems is of the order of intensity which is important to mental health research.

Proposed Course of Project: To continue such investigations of the electrical stimulation of behavior and of learning and eventually to relate the results to elicitable and spontaneous electrical activity in the various regions of the brain. To continue the work on the monkey, to expand the work to the chimpanzee, and to continue the work on the porpoise. At some time in the future we foresee that we will have progressed far enough in technical matters to apply these methods to the human.
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project: None

Honors and Awards relating to this project:

John C. Lilly: Invitation to serve as Secretary of the First Conference on the Use of Depth Electrodes in the Human. Georgetown Medical School, 10-13 June 1957.
Organizations of a conference on the use of depth electrodes in human patients which was supported under the auspices of the National Institute of Mental Health and the National Institute of Neurological Diseases and Blindness through Georgetown University Medical School; Dr. Francis M. Forster kindly consented to arrange for Georgetown to sponsor such a conference June 10-13, 1957. Dr. Desmond O'Doherty carried out the technical details of housing, organization of space, arranging for banquet, meals, etc. The Conference was attended by these principal investigators: M. Baldwin, R. G. Bickford, J. V. Brady, M. A. B. Brazier, W. P. Chapman, G. E. Chatrian, J. M. R. Delgado, H. W. Dodge, Jr., R. Galambos, H. Hamlin, R. G. Heath, W. J. H. Nauta, J. Olds, H. Patton, C. W. Sem-Jacobsen, E. A. Spiegel, A. Torkildsen, J. M. Van Buren. It was found to be of considerable value in mutual education among the participants as to (1) technical results, (2) indications for future research, (3) possible therapeutic values, (4) the dangers in employing such methods on the human, (5) improvement of methods in the future, (6) plans for a future conference, (7) methods of increasing the accuracy of localization within the human brain of the sites stimulated and recorded from.

Significance of this conference seems to be that there are a sufficient number of people working on the human brain with implanted electrodes and the results are sufficiently important at the present time to warrant interest on the part of the National Institute of Mental Health. It looks as though, with the methods devised up to the present time, that such methods are going to become relatively popular whether this is warranted therapeutically at present or not. It looks as if it is important to encourage publication and discussion and not to allow ethical judgments to drive people "underground", i.e. to prevent publications and full exchange between investigators. This field seems to be acquiring a respectability and a set of ethics which are acceptable to most of the medical profession and to most scientific investigators in the field.

It is generally agreed that indications for use of depth electrodes in a given patient are (1) cases of epilepsy without obvious lesions in the cortex and who are not amenable to drug treatment: for exploratory searching for deep foci of pathological
activity, (2) mentally ill cases in which there is a threat of removal of the frontal lobes in order to render them more amenable to custodial care, (the depth electrodes are very much less damaging, and exploratory investigation of such patients may show a more powerful therapeutic intervention can be brought about by electrical stimulation of local regions rather than sacrifice of such important areas of the brain), (3) those cases of severe neurological disease in which some sort of intervention is needed, such as in Parkinsonism, to prevent an irreversible clinical course by removal of foci such as those which occur in the globus pallidus; the investigation by electrical stimulation of such cases is warranted in view of the definite therapeutic advantage of such intervention as has been demonstrated by several neurosurgeons. These three justifications were brought out intensively at the conference and discussed at great length. The dangers of such intervention were brought out very strongly by the neurosurgeons present and improved methods were emphasized and the accounts of at least one death due to the employment of improper technical procedures was reported. The results on animals which were highlighted at the conference tentatively suggested to some of those present that eventually extremely powerful changes presumably can be brought about by electrical and chemical stimulation within the human brain, not only in cases of mental illness but presumably in psychosomatic illness also. These are some of the speculations which were exchanged at the conference in addition to the solid results which were presented.

A Steering Committee was set up with Desmond O'Doherty, Chairman, John C. Lilly, Secretary, and members as follows: R. G. Bickford, M. A. B. Brazier, J. D. French, R. G. Heath, C. W. Sem-Jacobsen and E. A. Spiegel.

Dr. J. D. French suggested a second conference be held at the new University of California Seminar Site at Lake Arrowhead, California, near Los Angeles.
NATIONAL INSTITUTE OF MENTAL HEALTH

Basic Research
Laboratory of Neurophysiology
Limbic Integration and Behavior

BUDGET SHEET

Estimated Obligations for FY 1958

Total: $144,864
Direct: $111,307
Reimbursements: $33,557

Projects included: M-NP-LI 1 and M-NP-LI 2
Part A.

Project Title: Studies on Localization of Function in Limbic System
I. Effects of Biochemically Induced Lesions

Principal Investigator: Paul D. MacLean, M.D.

Other Investigators: Richard E. Coggeshall, M.D.

Cooperating Units: None

Man Years
Total: 1.0
Professional: 0.6
Other: 0.4

Patient Days: None

Project Description:

Objectives: Lesions of the mammillary bodies and other subcortical structures of the limbic system are known to occur in association with Vitamin B deficiency. The administration of acetyl pyridine, an antimetabolite of nicotinamide, has been reported to result in acute neuronal degeneration in the archicortex (hippocampus), but not the neocortex; the supraoptic nuclei also undergo degeneration. The foregoing findings suggest a means of inducing lesions throughout integral parts of the limbic system for the purpose of studying behavioral changes. As selective damage of neurons throughout discrete cerebral structures is not possible to obtain by other methods, this investigation is being undertaken to evaluate the possibilities of this kind of an approach in studies on functional localization.

Methods Employed: (1) Mice and rats are being used in the initial studies. The first series of experiments are concerned with controlling the variety and extent of lesions induced by Vitamin B deficiency and the administration of acetyl pyridine. The brains of treated animals are being compared histologically with those of controls. In addition to the conventional staining of cells and fibers, the Nauta silver stain
will be used for tracing fibers of degeneration. (2) If it proves possible to obtain reproducible lesions, a study will be made of the effects of these lesions on the behavior of animals in a variety of psychological tests, including conditioned avoidance and delayed response tests.

Major Findings: Serial sections have been cut and stained on brains of control animals, as well as of a group of mice that were maintained on a Vitamin B deficient diet for one month. No lesions were found in the brains of the experimental group. Another group of animals that is being fed another variety of Vitamin B deficient diet is awaiting study. The brains of a number of acetyl pyridine treated rats is in the process of being sectioned, stained, and examined.

Significance to Mental Health Research: There already exists evidence that the structures under investigation are concerned in emotional and memory processes. Besides adding to basic knowledge needed in regard to localization of function in the limbic system, the present investigation has the potentiality of yielding information that will be useful to neuropharmacological investigations concerned with the differential action of drugs on nervous centers. It also has unique possibilities for contributing to the knowledge of anatomical connections of the limbic system.

Proposed Course of Project: If the results on mice and rats prove promising, the investigation will be extended to include observations on squirrel monkeys.

Part B included

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Project Title: Studies on the Limbic System

Principal Investigator: Paul D. MacLean, M.D.

Other Investigator: None

Cooperating Units: None

Man Years: Patient Days: None
Total: 0.2
Professional: 0.1
Other: 0.1

Project Description:

Objectives: During the period when the new section on Limbic Integration and Behavior is waiting to move into its full complement of space, part of the principal investigator's time is being devoted to completing six papers for publication. These papers, which deal with experimental work that was performed in the Departments of Physiology and Psychiatry at the Yale University School of Medicine, are as follows:

1. Effects of hippocampal seizures on conditioned avoidance behavior. (with Drs. J.R. Stevens and C. Kim)

2. Behavioral changes associated with chemical and electrical stimulation of the caudate nucleus. (with Dr. J.R. Stevens)

3. EEG and behavioral changes following chemical and electrical stimulation of posterior cingulate gyrus. (with Dr. W. Lockhart)

4. Effects of neuropharmacological agents on bioelectrical activity of limbic system. I. Reserpine and drugs of related interest. (with Dr. C. Kim)

5. Effects of neuropharmacological agents on bioelectrical activity of limbic system. II. Ether, nitrous oxide, and carbon dioxide. (with Dr. C. Kim)
Part A. (continued)

6. Propagation of hippocampal seizures in unrestrained and waking animals. (with Dr. C. Kim)

Major Findings: (1) Animals trained in a shuttle box to avoid a shock following the sound of a buzzer fail to respond to the conditioned stimulus during propagating hippocampal seizures, but in the majority of instances will quickly direct their escape upon receiving the unconditioned stimulus. (2) Either chemical or electrical stimulation of the head of the caudate nucleus interferes with the performance of an animal trained in conditioned avoidance. (3) Chemical stimulation of the cortex just above the posterior cingulate gyrus may result in spontaneous or easily induced penile erections in male cats. (4) The administration of reserpine to cats in a dose of one mg. per kg. results in distinctive electroencephalographic changes that can be localized to parts of the hippocampus and hypothalamus. (5) Except for the extended time course, the electroencephalographic picture associated with reserpine has many similarities to that observed during the induction and recovery stages of ether anesthesia. (6) The pattern of propagation of electrically induced hippocampal seizures in unrestrained and waking animals conforms to and confirms what has been found in acute preparations.

Significance to Mental Health Research: Experimentation during the past two decades has yielded evidence that allows one to infer a dichotomy in the function of the phylogenetically old (limbic) and new cortex. This dichotomy has important implications for neurology and psychiatry because it bears on the distinctive attributes of emotional and intellectual behavior. The papers in preparation shed further light on functional, electroencephalographic, and chemical distinction between the "old" and "new" cortex.

Proposed Course of Project: Completion within the near future.

Part B included Yes X No
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:

MacLean, P.D., Chemical and electrical stimulation of hippocampus in unrestrained animals. Part I. Methods and EEG findings. Arch. Neurol. and Psychiat., 1957, 78, 113-127.

MacLean, P.D., Chemical and electrical stimulation of hippocampus in unrestrained animals. Part II. Behavioral findings. Arch. Neurol. and Psychiat., 1957, 78, 128-142.


MacLean, P.D., "Psychosomatics", Handbook of Physiology. (in press)


Honors and Awards Relating to this Project:

1. Senior Postdoctoral Fellowship from the National Science Foundation. (Affiliated with the Physiological Institute, University of Zürich)

2. Invitation to become Associate Editor of Psychosomatic Medicine.

3. Invitation to speak at the Neurological Clinic, University of Freiburg, Freiburg, Germany.

4. Invitation to speak to the neurological and neurosurgical groups at the University of Graz, Graz, Austria.
Part B (continued)


6. Invitation to write a review on the limbic system for Physiological Reviews.

7. Invitation to serve as a member of the Selection Committee of the National Institute of Mental Health.
ESTIMATED OBLIGATIONS FOR FY 1958

Total: $97,008
Direct: $74,536
Reimbursements: $22,472

Projects included: M-NC-PC 1 through M-NC-PC 9
Project Title: Structure of Transition-Metal Complexes

Principal Investigator: Gary Felsenfeld

Other Investigators: Leslie E. Orgel

Operating Units: None

In Years
Total: 1/4
Professional: 1/4
Other:

Project Description:

Objectives: To study by theoretical methods the unusual configurations of certain transition-metal complexes.

Methods Employed: The quantum-mechanical method known as the crystal-field theory was employed.

Major Findings: It has been shown in a previous investigation by G. Felsenfeld that the unusual flattened tetrahedral configuration of the complex ion CuCl₄⁻ can be explained theoretically. The present research has extended the study to a consideration of complexes of nickel, and it has been shown that for a complex ion of the form NiCl₄⁻ an elongated tetrahedral configuration is to be expected. The amount of distortion has been predicted.

Significance to Mental Health Research: The role of metal ions in biological systems depends upon the directional properties of the bonds they form. The understanding of the activity of the metal-containing enzymes of ceruloplasmin and of cerebrocuprein all depend upon a knowledge of the stereochemistry of the metal ion involved. Theoretical studies permit us to predict the behavior of such ions under varying conditions.

Proposed Course of Project: Calculations will be extended and refined to take into account further energy terms. In collaboration with D. R. Davies, X-ray diffraction studies of nickel chloride complexes will be undertaken to verify the predictions of the theoretical study.

Included Yes X No
B: Honors, Awards, and Publications

Publications other than abstracts from this project:

Felsenfeld, G. and Orgel, L. E., "Jahn-Teller Distortions of Tetrahedral Transition-Metal Complexes". In preparation.

Honors and Awards relating to this project: None.
A.

Project Title: Physical Chemical Studies on Synthetic Polyribonucleotides.

Principal Investigator: Gary Felsenfeld

Other Investigators: Alexander Rich, David R. Davies

Cooperating Units: None

Man Years
Total: 1-1/2
Professional: 1-1/4
Other: 1/4

Project Description:

Objectives: To study behavior of various synthetic polyribonucleotides.

Methods Employed: The synthetic polynucleotides have been examined spectrophotometrically, and with the ultracentrifuge. Theoretical techniques have been applied for discussing the statistics of interaction of the polymers.

Major Findings: The study of the interaction between polyadenylic acid (poly A) and polyuridylic acid (poly U) has been continued. A new three-stranded molecule, involving two strands of poly U for each strand of poly A has been discovered using techniques like those which led to the discovery of the two-stranded molecules. This three-stranded molecule may be related to a structure (as yet undetected) involving a single ribonucleic acid (RNA) strand wrapped about a two-stranded desoxyribonucleic acid (DNA), and is therefore of considerable interest with relation to problems of nucleic acid synthesis.

The dependence of the formation of multiple-stranded structures on concentration of small ions has also been studied. It is found that small amounts of divalent cation (Mg$^{++}$, Mn$^{++}$, etc.) are sufficient to cause formation of the two-stranded complex, whereas large excesses of cation concentration are required for addition of the third strand. The dependence of two-stranded polynucleotide stabilization upon ion concentration closely resembles that found for DNA.
Part A (Continued)

Theoretical studies have also been carried out to determine whether the observed experimental data for formation of two-stranded complexes can be explained either on basis of a rapidly reversible or an irreversible process. It has been shown by means of these studies that only a system involving highly labile bonds between the two strands can account for the data. This suggests that two-stranded DNA is also capable of a very rapid dissociation reaction, a consideration of great importance for proposed mechanisms of DNA replication, which involve separation of the two strands as part of the process.

Significance to Mental Health Research: These synthetic polymers are models of RNA and DNA, and provide a means of studying reactions of the nucleic acids under well-defined chemical conditions.

Proposed Course of Project: Continued combined theoretical and experimental studies will be undertaken to determine the mechanism of interaction between poly A and poly U, and between other polynucleotides.
Publications other than abstracts from this project:


Honors and Awards relating to this project: None.
Project Title: The Formation of a New Helical Complex between Polyinosinic Acid and Polyadenylic Acid.

Principal Investigator: David R. Davies

Other Investigators: Alexander Rich

Operating Units: None

Year
Total: 1/2
Professional: 1/2
Other:

Project Description:

Objectives: To define the conditions under which these synthetic polynucleotides interact, and to discover the nature of the complex formed.

Methods Employed: Ultra-violet absorption and ultracentrifugation techniques have been employed to examine the conditions under which the complex forms. X-ray diffraction methods were used to investigate the structure of the complex.

Major Findings: It has been discovered that polyinosinic acid and polycytidylic acid will combine rapidly in solution to form a helical molecule. X-ray diffraction photographs show that, contrary to expectation, this molecule is dissimilar to that formed when polyadenylic acid and polyuridylic acid react together. The structure, in fact, appears to be very similar to that of natural ribonucleic acid (RNA). One implication of this finding is that the RNA molecule exists in an even-stranded helical configuration, at least under the conditions used for X-ray diffraction studies. It is to be expected that the elucidation of the structure of this molecule will throw considerable light on the RNA structure which is at present undetermined.

The reaction takes place rapidly in the presence of 0.1 M sodium chloride. It is inhibited by the absence of sodium chloride and by the presence of 1.0 M sodium chloride. Ultra-centrifuge studies show that the complex sediments much faster than either of the separate polymers.
Project Description (Continued):

Significance to Mental Health Research: An understanding of the role played by RNA in cellular metabolism is basic to our understanding of cell differentiation and function. RNA is involved in protein synthesis and most current hypotheses about protein synthesis invoke the use of RNA as the template on which the amino acids are ordered. Knowledge of the structure of RNA is therefore important, since this will clarify our understanding of the manner in which it can act as such a template. The structure of natural RNA is difficult to obtain directly, whereas much clearer information concerning the configurations of molecules of this type has been obtained from studies such as this on the synthetic polynucleotides.

Proposed Course of Project: Further work will be carried out to obtain better X-ray diffraction patterns of this complex with a view to elucidating its structure. Further investigations will also be undertaken to define the condition under which the complex is stable.
Honors, Awards, and Publications

Publications other than abstracts from this project:


Honors and Awards relating to this project: None.
Project Title: Computation of helical Transforms for Synthetic Polypeptides.

Principal Investigator: David R. Davies

Other Investigators: Alexander Rich

Cooperating Units: None

Man Years
Total: 1/2
Professional: 1/2
Other: None

Project Description:

Objectives: To study various proposed helical polypeptide models by means of the helical transform computation.

Methods Employed: The helical transform computation yields a theoretical X-ray diffraction pattern for proposed molecular structures. Use of this technique provides a basis for comparison with the observed diffraction data.

Major Findings: The α-helix is of considerable importance since it is now generally believed to be the basic structural unit, not only of the synthetic polypeptides and the fibrous proteins, but also of many globular proteins. It was therefore considered interesting to examine the diffraction patterns of other helices (notably, the π-helix) to see whether they were markedly different from those of the α-helix. A careful examination shows that for the synthetic polypeptides, a clear distinction can be made in favor of the α-helix. However, this investigation demonstrates that such a clear distinction cannot be made for the natural fibrous proteins.

Further computing programs have also been developed for rapid calculation of interatomic distance and angles in helical molecules.
Part A. (Continued)

Significance to Mental Health Research: This investigation has led to further understanding of the relation between the configurations assumed by proteins and their X-ray diffraction patterns.

Proposed Course of Project: This project has been completed.

Part B Included Yes X No
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:


Honors and Awards relating to this project: None.
Project Title: Physical Properties of Ribonucleic Acids

Principal Investigator: Dan F. Bradley

Other Investigators: Jean Johnson

Cooperating Units: None

Man Years
Total: 3/4
Professional: 1/2
Other: 1/4

Project Description:

Objectives: Much attention has been focussed in recent years on ribonucleic acids (RNA) because they seem to be intimately associated with in vivo protein synthesis. Their function in this process rests upon the fact that they are linear, unbranched polymers, presumably varying from one to another both in polymer length and rigidity. For several years we have been accumulating evidence as to how these properties change spontaneously in samples of RNA during and subsequent to isolation from organisms. These studies lead to better understanding of the structure of native RNA and how it can be isolated for study with a minimum of alteration. This work is also relevant to the paradox of the apparent in vivo stability and in vitro lability of nucleic acids and the problem of stabilizing these genetic materials against radiation damage.

Methods Employed: Ultracentrifugation, ultraviolet spectrophotometry, column chromatography, electrophoresis, viscosity.

Major Findings: Two major avenues of approach have been followed. One has been the careful study of the relative lability of a particularly promising RNA in aqueous solutions as a function of ionic environment. The addition of small amounts of divalent cations to RNA solutions in ion-free water lowers the optical absorption of the RNA (an indication of increasing polymer rigidity) as well as retards the fall of sedimentation coefficient upon standing at moderately elevated temperatures. Monovalent cations perform the same stabilizing functions but at much higher concentrations suggesting that they interact less strongly with the RNA because of their lower ionic charge.
At temperatures approaching 100°, the ion-RNA complexes begin to dissociate as indicated by increased optical absorption. Under these conditions, the monomer-monomer linkages in RNA are ruptured by polycations so that under these conditions RNA is labilized by divalent cations.

Another avenue followed has been the isolation of RNA from a source (rabbit muscle) which provides unusually difficult isolation problems. This work was carried out in collaboration with Dr. E. Mihalyi and Miss Irene Knoller of the National Heart Institute. As is true will all RNAs studied to date, the product was heterogeneous, having a distribution of chain lengths and flexibilities. Most interestingly, application of normal isolation procedures resulted in removal of a non-random fraction. Therefore the mean values of the properties of RNAs isolated by different methods varied because part of the RNA was discarded, although normally, this variation would be ascribed to alterations of the RNA during isolation. Such changes were also observed. Further, it was discovered that the chromatographic technique we developed for separating RNA into various chain lengths is also suitable for separating RNA from protein contaminants.

Significance to Mental Health Research: This study is part of a long-term group effort to discover the mechanisms of protein synthesis and genetic transfer.

Proposed Course of Project: There is recent evidence that cerebral RNA varies with mental state. We intend to isolate ribonucleoprotein particles from animal brain and see whether they are in any way different from the corresponding protein-synthesizing particles found in liver.

We are also interested in searching for methods to separate low molecular weight RNAs to investigate their optical properties, their binding of cations, and their binding to other nucleic acids.
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:


Honors and Awards relating to this project: None.
Project Title: Frictional Properties of Desoxyribonucleic Acid in Solution.

Principal Investigator: Dan F. Bradley

Other Investigators: None

Cooperating Units: None

Man Years:
Total: 1/2
Professional: 1/2
Other:

Project Description:

Objectives: Desoxyribonucleic acid (DNA) has been shown to carry genetic information. As DNA is a linear, unbranched polymer consisting of four different monomer units, this genetic information is presumably coded along the polymer chain by variations in the sequence of monomers. It follows that a longer polymer chain can code a larger amount of genetic information. A great deal of effort has been expended to measure the chain length of DNA in solution either by light scattering or by frictional methods. The latter methods which measure the rate at which DNA molecules move through a solution under different applied forces do not agree with the former methods. In the present study the relationships between the frictional properties and the polymer length of DNA are reexamined.

Methods Employed: A careful survey of the literature on experimental determinations of the chain length of DNA revealed that a heretofore unobserved simple relationship existed between the chainlength (or molecular weight, M) of DNA and the velocity with which it moves in a centrifugal field (sedimentation coefficient, S), i.e. \( M \propto S^{2.79} \). This was significant because heretofore an additional frictional measurement (such as viscosity or diffusion) was believed to be necessary to calculate M from S data. Upon further examination of the data, however, it became apparent that the equations used to extrapolate the observed S data to the
Part A. (Continued):

Theoretically meaningful state of infinite dilution were neither theoretically justifiable in themselves nor even fit the experimental S data in the measured concentration range. A theory was developed to explain the observed variation of S at finite concentrations and provide a satisfactory extrapolation to infinite dilution.

Major Findings: The theory developed accounts for the observed decrease in sedimentation rate at finite concentrations in terms of a reverse flow of solvent, required by conservation of volume conditions. The DNA actually flows faster relative to solvent than as measured by a stationary observer. The theory thus includes terms for the volume of DNA, the amount of solvent which it carries along with it, and the degree to which it is permeable to the solvent. DNA is a relatively rigid polymer and wanders through, or "occupies" thousands of times its own molecular volume. Hence its permeability to solvent molecules is unusually high, a fact which increases the frictional drag on the molecule and makes the relation between chain length and frictional properties obscure.

When observed S-concentration data were fitted to the theoretical expression, a remarkably good fit was achieved. The values of the parameters for volume, hydration, permeability, and S at zero concentration (S.) are of reasonable magnitudes, while the volume "occupied" agree within a few percent of the value calculated from viscosity data. The values of S, and volume occupied may be combined with any of the existing theories to calculate molecular chain lengths without resort to any additional frictional measurement.

Significance to Mental Health Research: This study is part of a long-term group effort to discover the mechanisms of protein synthesis and genetic transfer.

Proposed Course of Project: Molecular sizes may be calculated from S vs. concentration data using existing theories. However, these theories treat only limiting cases of complete permeability or impermeability, whereas DNA is approximately halfway between these extremes. An effort is being made to develop a theory which will treat this intermediate case. One reason why this case has not been treated previously is that prior to the theory discussed above there was no method for estimating permeability of highly extended polymer molecules. The theory applies generally to all such molecules and we hope to extend its application to other cases such as RNA, synthetic polynucleotides, and nucleoproteins.
Project Title: Structure of a Complex Formed Between Polyadenylic Acid and Polyinosinic Acid.

Principal Investigator: Alexander Rich

Other Investigators: None

Cooperating Units: None

Man Years
Total: 1/4
Professional: 1/4
Other:

Project Description:

Objectives: To discover the configuration assumed by the synthetic polyribonucleotides polyadenylic acid and polyinosinic when they combine together to form a helical complex.

Methods Employed: Principal methods in this investigation are those of X-ray diffraction. Ancillary methods include spectrophotometric studies, ultracentrifugal studies, and titration curves.

Major Findings: It has been discovered that in dilute aqueous salt solutions, polyadenylic acid will combine with polyinosinic acid to form a two-stranded helical complex. In addition, it has been found that this two-stranded helical complex will take on a third polyinosinic acid molecule to form a three-stranded helical complex. This reaction is controlled by the ionic conditions of the environment. Thus, in solutions with a salt concentration less than $10^{-5} \text{ M}$, no reaction occurs at all. In solutions which are 0.1 M in NaCl, the reaction occurs very rapidly, resulting in the formation of the three-stranded complex within four minutes. If the salt concentration is reduced, however, to 0.01 M, then the reaction proceeds more slowly, and one can clearly differentiate the initial formation of the 1:1 complex of polyadenylic acid and polyinosinic acid followed by the subsequent addition of a polyinosinic acid molecule to form a final complex which is 2:1 with two polyinosinic acid molecules and one polyadenylic acid molecule.
An X-ray diffraction photograph has been obtained of the 1:1 complex which clearly shows that it is a helical molecule with a pitch of 38.8 Å. These molecules are parallel to each other and packed together in a hexagonal array. Work has been done in the elucidation of the structure of the two-stranded complex. At the present time, it is believed that this complex forms by having the two purine bases hydrogen bonded together and the base pairs packed together helically with the ribose phosphate chains on the outside of the molecule.

**Significance to Mental Health Research:** Ribonucleic acid is a molecule found in all nervous tissues and is currently believed to be an essential ingredient for the synthesis of protein. The synthetic polyribonucleotides are molecules which have the same ribose phosphate backbone as is found in ribonucleic acid itself, and by studying the configurational potentialities inherent in these synthetic polymers, we can determine the configurational possibilities which are open to RNA itself. In this way, we hope to elucidate the fundamental mechanisms of protein synthesis, a mechanism which will be applicable to these protein synthetic activities within nervous tissue as well as in other tissues.

**Proposed Course of Project:** This work will be continued by carefully studying the diffraction patterns produced by the various models of the type described above. In addition, the models will be built for the three-stranded helical complex.

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**Part B Included**

Yes [X]  No ___

- 233 -
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:


Honors and Awards relating to this project: None.
Part A.

Project Title: Determination of the Structure of Collagen

Principal Investigator: Alexander Rich

Other Investigators: F.H.C. Crick

Cooperating Units: None

Man Years
Total: 1/4
Professional: 1/4
Other:

Project Description:

Objectives: To determine the configuration of collagen and related proteins.

Methods Employed: Principal method used in this investigation is that of X-ray diffraction. Diffraction patterns are obtained from stretched samples of collagen or tendon or of elastin. These diffraction patterns are then analyzed, using a computer for calculating the diffraction patterns expected from various helical structures.

Major Findings: Two years ago, these investigators proposed a model for the structure of collagen. This proposal has been accepted in the intervening two years by all of the investigators working in the collagen field. At the present time, we are expanding the work on collagen to work out various fine features in the structure of the molecule. Thus, we have been spending a great deal of time on the configuration and position of the various amino acid side chains which are known to exist in the collagen molecule. In addition, we have found several hydrogen bonded side chain linkages which are believed to be of importance in the lateral stabilization of the molecules when they are parallel to each other. Among other things, these investigations proved useful in understanding the mechanism of tanning. In the tanning process, metal ions are introduced between the parallel collagen molecules and by complexing onto amino acid side chains from adjoining molecules, the neighboring units are firmly held together so that they can no longer separate. This results in a tanned collagen fiber.
Part A. (Continued)

In addition, some work has been done on stretched elastin fibers. Elastin is a protein which has an amino acid composition somewhat similar to collagen, but has a structure which has not been determined as yet. For various reasons, we have felt that the elastin molecule has a degenerate collagen structure, and attempts have been made to re-orient elastin so as to demonstrate its close relationship with collagen. A certain measure of success has been achieved along these lines.

Significance to Mental Health Research: Collagen is the major tensile element which is found in the animal kingdom. In addition to being spread through all the phylla, it is equally well distributed through all the tissues of the body, including the nervous system. There, collagen is found in the fibrous wrappings around nerves as well as in the fibrous covering of blood vessels in the central nervous system. Through a fundamental understanding of the configuration of collagen molecule, we hope to better understand the role which it plays in holding tissues together.

Proposed Course of Project: This work will be continued along lines described above.
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:


Honors and Awards relating to this project:

An invitation to present the opening paper at an International Conference on Collagen and Gelatin, held in Cambridge, England July 1 through 7, 1957.
Part A.

Project Title: Investigation of the Structure of Steroid Amino Acid Complexes.

Principal Investigator: Alexander Rich

Other Investigators: David M. Blow

Cooperating Units: None

Man Years
Total: 1/2
Professional: 1/2
Other:

Project Description:

Objectives: To determine the structure of the molecular complexes which form between desoxycholic acid and various amino acids and polypeptides.

Methods Employed: The principal tool used in this investigation is X-ray diffraction. Other subsidiary tools are spectro-photometric analyses, viscosity studies, freezing point depression, and pycnometry.

Major Findings: We have discovered that a steroid molecule, sodium desoxycholate, will form a series of helical complexes in the presence of a variety of amino acids or polypeptides. X-ray diffraction studies of these complexes show a remarkably detailed and precise organization of the flat steroid molecule and the amino acid residues. The crystallographic investigation has shown that these molecules form a complex with a diameter of approximately 40 Å. Thus, it is quite likely that the flat steroid molecules lie adjacent to each other with amino acids between them. This statement is supported by the finding that additional amino acids added to the complex are usually located on the periphery of the complex.

A series of investigations has been carried out to determine the stoichiometry of the interaction between the steroid and amino acid. These have shown that the optimum ratio is one steroid molecule to one amino acid. The complex will continue to form if there is an excess of amino
acids, however, as, for example, going up to a mole ratio of 3 or 4 to 1. In the presence of additional steroids, however, the complex failed to form. Thus, if there are more than two steroid molecules per amino acid, no complexes form at all. This effect can be shown very markedly in viscosity study of these complexes in solution.

Eight amino acids and five peptides have been studied thus far. It has been shown that all of them will interact with a steroid, either through a marked increase in the viscosity of solution or by the production of a characteristic X-ray diffraction photograph.

**Significance to Mental Health Research:** A large component in the nervous system are the steroid molecules which are found largely in the myelin. Very little is known regarding the structural role which these flat molecules play in organizing the myelin sheath. The purpose of this study is to show how the closely related steroid molecule, sodium desoxycholate, interacts with amino acids in the hope that it will throw some light on the role which steroids play in the nervous system.

**Proposed Course of Project:** Studies will be continued along the lines described above until the complete structure analysis has been worked out.

**Part B Included**

Yes [ ] No [X]
Basic Research
Laboratory of Cellular Pharmacology

BUDGET SHEET

Estimated Obligations for FY 1958

Total: $358,362
Direct: $275,350
Reimbursements: $83,012

Projects included: M-CP 1 through M-CP 15
Project Title: Methionine Activating Enzyme in Rabbit Liver

Principal Investigator: Giulio L. Cantoni, M. D.

Man Years
Total: 1-1/3
Professional: 1/3
Other: 1

Project Description:

Objectives:

Mammals, plants and fungi and presumably other phyla utilize the methyl group of methionine for biological methylations. As a result of recent work on the mechanism of transmethylation reactions, it has been established that in reality activation of methionine is a prerequisite to the transfer of its methyl group. Biologically the activation reaction is catalyzed by an enzyme found in yeast and in the liver of numerous mammalian species. In this reaction, adenosine triphosphate plays an essential role; specifically adenosine triphosphate fulfills a dual function inasmuch as it serves a) directly or indirectly as a donor source of its adenosine moiety, which is incorporated in "active methionine", and b) as an energy source, since it has been calculated that the methyl-sulfonium bond in "active methionine" is roughly equivalent to the pyrophosphate bond in adenosine triphosphate.

Major Findings:

Repeated efforts were directed toward the separation of the activity of the methionine activating enzyme into two or more protein fractions. All these attempts were uniformly negative. Furthermore attempts at recombination of protein fractions from rabbit liver with protein fractions obtained in the course of purification of the methionine activating enzyme from yeast (Project M - CP 2) were likewise
negative. While evidence of this kind is not compelling, all indications suggest that the formation of S-adenosylmethionine from methionine and ATP is catalyzed by a single protein moiety.

Significance to Mental Health Research:

This project is part of a larger study of biological methylations. The role of transmethylation reactions of biogenesis of neuro-hormones such as acetylcholine and epinephrine, metabolites important in neuro-muscular functions like creatine and anserine and of pharmacologically active agents like bufotenine, mescaline and many other alkaloids clearly indicates that this broad area of research is of significance to basic research in neurology and mental health.

Part B included Yes / /

No / /
Project Title: Studies on Methionine Activating Enzyme of Yeast.

Principal Investigator: S. Harvey Mudd, M. D.

Man Years
   Total: 1-2/3
   Professional: 2/3
   Other: 1

Project Description:

Objectives:

The objectives of the project have been outlined in a previous annual report. Briefly, these are to further elucidate the detailed mechanism of the enzymatically catalyzed formation of \( S\)-adenosylmethionine, the compound which serves as a biological donor of labile methyl groups and of certain aliphatic carbon chains.

Major Findings:

The methionine activating enzyme has been extracted from bakers' yeast and purified 250-fold from this extract by one method and 200-fold by a second method. The properties of the enzyme in regard to stability, pH effects, substrate specificity for methionine and adenosine triphosphate, and the effect of various inhibitors have been studied. Cofactor requirements for both a monovalent and divalent cation have been demonstrated and the specificity of these requirements investigated. The stoichiometry of the reaction and the reaction products have been studied. By use of \( P^{32} \) labelled adenosine triphosphate the method of breakdown of this substance has been clarified. An important negative finding has been the failure of the enzymatic activity to fractionate into two or more protein moieties during extensive purification.

Significance to Mental Health Research:

This project is part of a larger study on biological methylations, the significance of which to mental health has been discussed elsewhere. In addition, the purification of this enzyme from yeast
allows detailed comparison with the previously purified analogous liver enzyme, a comparison which is especially important from the viewpoint of comparative biochemistry.

Part B.

Mudd, S. H., and Cantoni, G. L.
"Activation of Methionine for Transmethylation III. The Methionine Activating Enzyme of Baker's Yeast" J. Biol. Chem., in press

Mudd, S. H., and Cantoni, G. L.
"Selenomethionine in Enzymatic Transmethyllations" Nature, in press
A.

Project Title: Study of methionine synthesis by enzymatic transmethylation from betaine or dimethylthetin.

Principal Investigator: Jack Durell, M. D.

Other Investigators: Giulio L. Cantoni, M. D.

Man Years
Total: 1-1/2
Professional: 5/6
Other: 2/3

Project Description:

Objectives:

To study the mechanism of the enzymatic transfer of alkyl groups from "onium" poles and the energetics of such reactions; to investigate whether two enzymes are involved to characterize their properties and substrate specificities.

Major Findings:

As reported in 1956 homocysteine-thetin-methylpherase, HTMP, has been purified to the point where it appears to be almost pure. The purified enzyme undergoes an interesting and novel polymerization reaction which can be reversed with a variety of sulphydryl compounds. The kinetics and mechanism of this reversible polymerization reaction has been investigated in detail by biochemical and physicochemical means, in part in collaboration with Dr. R. Steiner of NMRI.

With the purified enzyme it has been possible to measure by direct calorimetry the enthalpy change in the methyl transfer reaction from dimethylthetin. The $\Delta H$ was found to be $-12000$, indicating a very large change in the standard free energy of the reaction. This aspect of the work was carried out in collaboration with Professor Julian Sturtevant of Yale University.
Interesting though preliminary results on the relationship of HTMP to the enzyme catalyzing the synthesis of methionine from betaine and homocysteine were obtained and will be pursued further.

Significance to Mental Health Research:

This project is part of a larger study on biological methylations. As is well known, "onium" compounds have profound pharmacological effects upon the nervous system and it has been suggested that they may play a role in the conduction and transmission of the nervous impulse. Knowledge of mechanisms of synthesis and degradation of such compounds as well as the energetics of such reactions might therefore contribute to our understanding of nervous tissue function.

Part B.

Durell, J., Anderson, D.G., and Cantoni, G.L.
"The Synthesis of Methionine by Enzymic Transmethylation
I. Purification and Properties of Thetin Homocysteine Methylpheras"
Biochim. and Biophys. Acta, in press

Durell, J. and Sturtevant, J.M.
"The Synthesis of Methionine by Enzymic Transmethylation
II. Enthalpy Change in the Methyl-Transfer from Dimethylacetotheti"
Biochim. and Biophys. Acta, in press
A.

Project Title: Metabolism of S-Adenosyl-L-homocysteine (ASR).

Principal Investigator: Gabriel de la Haba, Ph.D.

Man Years
Total: 1-2/3
Professional: 2/3
Other: 1

Project Description:

Objectives:
This project is a continuation of last year's finding on the enzymatic synthesis of ASR by way of condensation of L-homocysteine and adenosine.

Methods Employed:
The enzyme involved has been purified about eighty-fold from rat liver by conventional methods of protein fractionation. The product of the reaction has been characterized chemically and enzymatically.

Major Findings:

It has been found that the enzymatic reaction between adenosine and L-homocysteine is very specific for both of the above-mentioned reactants; no other purine or pyrimidine nucleoside will substitute for adenosine, and no mercaptan other than L-homocysteine will react. Of interest also is the fact that the equilibrium of this reaction has been found to lie very far in the direction of condensation; the hydrolysis of ASR is however readily obtained with the same enzyme if both the products of the reaction are trapped enzymatically (a) adenosine with its specific deaminase, and (b) L-homocysteine with the enzyme homocysteine-thetin methylpherase which has been purified and studied extensively in this laboratory.

Chemical methylation of ASR to yield S-adenosyl-L-methionine was performed and enzymatic studies on the product undertaken. It has been found that in the chemical methylation only half of the S-adenosyl-L-methionine formed is active in the enzymatic
methylation of guanidoacetic acid to yield creatine. It appears that two stereoisomers of the sulfonium group are obtained upon methylation of ASR in agreement with organic chemical methylations of simpler thioethers. Further study of this finding is contemplated.

Significance to Mental Health Research:

This study is a part of the general problem of transmethylation reactions under investigation in this laboratory. ASR is a product of the transfer of methyl groups from active methionine to a number of acceptors such as guanidoacetic acid, nicotinamide, etc. It would appear that investigations on its fate--and as here described its biosynthesis--may add to our knowledge of the general problem of sulfur metabolism, sulfonium metabolism, and methyl transfer reactions metabolic processes which are acquiring increasing significance in neurochemistry.

Proposed Course of Project:

This project will be continued especially in conjunction with Project M - CP 12.

Part B included Yes / / No /x/
Project Title: Amino acid analogue studies of protein synthesis.

Principal Investigator: Michael Yarmolinsky

Man Years
Total: 2/3
Professional: 2/3
Other: -

Project Description:

Objectives:

(1) Selective inhibition of the capacity of pancreas tissue slices for the net synthesis of specific proteins by use of appropriate amino acid analogues.

(2) Investigation of the transfer of activated amino acid to its first acceptor prior to incorporation into protein in vitro.

Methods Employed:

(1) Pigeon pancreas slices were incubated in a nutrient medium. Increases in amylase activity following homogenization of the tissue slice in its incubation medium were investigated under various conditions. The initial amylase levels before incubation were determined by a method previously developed in this laboratory.

(2) Cell-free preparations of rat liver and of yeast were studied by measuring incorporations of radioactive pyrophosphate or adenylic acid into adenosine triphosphates in the presence and absence of amino acids.

Major Findings:

(1) In contrast to previous reports, but consistent with recent analyses of amylase composition, methionine was found to
stimulate slightly the synthesis of amylase by pigeon pancreas slices. Ethionine showed a questionable inhibition. Tryptazan can to a certain extent replace or spare the utilization of tryptophan for amylase synthesis.

(2) The report of an alanine-dependant, ribonuclease-inhibited adenylic acid incorporation into adenosine triphosphate by extracts of rat liver was not confirmed. Nor was it possible to demonstrate in yeast extracts an amino acid dependant incorporation of adenylic acid into ATP.

The sulfonic acid analogue of alanine is not activated.

Significance to Mental Health Research:

For growth and regeneration nerve tissue depends on the processes of protein synthesis which is the subject of these investigations.

Proposed Course of Research:

Owing to the extreme variability of the pigeon pancreas experiments, this aspect of the work has been discontinued. The work with cell-free systems will be continued in the coming year.

Part B included  Yes /✓/  No /x/
Project Title: The Conversion of Phenylalanine to Tyrosine.

Principal Investigator: Seymour Kaufman, Ph.D.

Other Investigators: Bruce Levenberg, Ph.D.

Years
Total: 1-2/3
Professional: 2/3
Other: 1

Project Description:

Objectives:

Almost nothing is known about the mechanism of biological hydroxylation reactions. For many compounds, including steroids and some drugs, hydroxylation is on the normal pathway of metabolism. For the essential amino acid, phenylalanine, hydroxylation to tyrosine represents a preliminary step prior to its complete oxidation via (ultimately) the citric acid cycle.

Methods Employed:

The methods employed in the problem are those of (classical) enzymology. For the separation and purification of the individual enzymes, such techniques as salt fractionation, organic solvent fractionation and selective adsorption and elution from gels have been employed. Spectrophotometric and chemical assays have been used to follow the course of the reaction.

Major Findings:

From kinetic studies previously carried out on this system, indications were obtained for the participation of another cofactor in this reaction, in addition to TPNH. This cofactor has now been isolated from
boiled extracts of rat liver. It has been shown that the lag period of the reaction which has previously been reported, can be eliminated by a short anaerobic incubation of TPNH with the cofactor in the presence of the highly purified sheep enzyme. These results suggest that there is an interaction between TPNH and the cofactor and that this reaction is catalyzed by the sheep enzyme as shown in the reaction (1):

\[ \text{TPNH} + \text{H}^+ + \text{X} \xrightarrow{} \text{TPN}^+ + \text{XH}_2 \]

In the subsequent reactions in what must obviously be a complex sequence, this reduced cofactor may be oxidized by molecular oxygen to form the primary hydroxylating agent. The rat enzyme probably participates in these later reactions involving the actual hydroxylation of phenylalanine.

Significance to Mental Health Research:

It is known that this reaction, the conversion of phenylalanine to tyrosine, is at least partially blocked in the disease oligophrenica phenylpyruvica. One of the characteristics of this disease is a severe impairment in mental ability. With an increased understanding of the nature of the reactions catalyzed by the 2 enzymes which are involved in this conversion of phenylalanine to tyrosine, it should be possible to delineate more precisely the nature of the biochemical abnormality of this disease.

Proposed Course of Project:

The work on the purification of the enzymes will be continued, mainly to explore the possibility that more than 2 enzymes are involved. The detailed mechanism of the reaction should be more amenable to study when larger amounts of the purified enzymes and the new cofactor become available.
Project Title: Hormonal Regulation and Protein Synthesis.

Principal Investigator: Seymour Kaufman, Ph.D.

Other Investigators: Louis Sokoloff, M.D.

Cooperating Units: M - CS - CM - 4

Man Years
Total: -
Professional: -
Other: -

Project Description:

Objectives:

Only recently methods have become available for studying protein synthesis in vitro. Utilizing these methods, it has been clearly demonstrated that protein synthesis is coupled to energy-yielding reactions in the cell. The mechanism of the synthesis and of this coupling are unknown. The objectives of this study are three-fold. (a) Investigate in general the mechanism of protein synthesis, (b) Attempt to elucidate the nature of the coupling of the energy supply and the synthetic reaction. More specifically, this system would seem to offer the possibility of investigating the question of whether or not different energy-yielding reactions are geared to specific synthetic reactions. Thus it is now known that during oxidation of substrates with molecular oxygen, energy is tapped from the hydrogen carrier system at three separate sites. It would be of great interest to know if the energy liberated at these three sites is equally available for all synthetic reactions. (c) To investigate the possible hormonal regulation of protein synthesis.
Part A. (Continued)

Major Findings:

During this year, the course of the problem has paralleled closely the work described in Project M - CS - CM - 4.

Part B included Yes /✓/ No /x/
A. Project Title: Studies on the Cofactor Required for the Enzymatic Conversion of Phenylalanine to Tyrosine.

Principal Investigator: Seymour Kaufman, Ph.D.

Man Years
Total: 1-2/3
Professional: 2/3
Other: 1

Project Description: See previous project

Objectives: See previous project

Methods Employed:

The cofactor has been purified from boiled extracts of rat liver by a combination of procedures including: Organic solvent fractionation, ion exchange chromatography and partition chromatography on silica gel columns.

Major Findings:

Enzymatic assays for the cofactor have been developed which can detect quantities of the material in natural materials. Using these assays, many tissues have been examined as possible starting materials for large scale isolation attempts. So far, activity has been detected only in liver and adrenal tissue. Of the livers tested (beef, sheep, rabbit, monkey, rat) rat liver has the highest activity. The cofactor has been isolated from this source by a procedure which leads to about 1000 fold purification. Extensive tests for specific chemical groups have been carried out and from the results of these tests, as well as from some of its physical properties, it can be concluded that the cofactor is an unstable heterocyclic organic base which contains 20-30 per cent nitrogen.

Significance to Mental Health Research:

There is good evidence that the conversion of phenylalanine to tyrosine is at least partially blocked in the disease, oligophrenia phenylpyruvica. With the realization that at least
2 enzymes are involved in this conversion, experiments have been reported which attempt to specify whether both or only a single enzyme is missing or blocked in the disease. The finding that a non-protein cofactor is also involved in this conversion raises the possibility that it is the cofactor which is missing in the disease.

Proposed Course of Project:

The purification and the studies of the structure of the cofactor will be continued. In addition, the possibility that it is the cofactor which is missing in oligophrenia phenylpyruvica will be investigated.

Part B.

Kaufman, Seymour  
"A New Cofactor Required for the Enzymatic Conversion of Phenylalanine to Tyrosine"  
J. Biol. Chem., in press
A.

Project Title: Clinical Studies on Phenylketonuria.

Principal Investigator: Seymour Kaufman, Ph.D.

Man Years
Total: 2/3
Professional: 1/3
Other: 1/3

Project Description:

Objectives:

It has been established that in this disease there is at least a partial block in the conversion of phenylalanine to tyrosine. In vivo studies have shown that in phenylketonuria only one of the 2 enzymes which are known to participate in this enzymatic system is missing. The possibility exists, however, that it is not an enzyme which is missing but rather a coenzyme which is required for the activity of this enzyme. Experiments will be carried out to test the possibility that it is the cofactor which is missing in the disease. If it is actually an enzyme lack, the studies on the mechanism of the normal enzymatic conversion of phenylalanine to tyrosine should allow for a better understanding of the nature of the metabolic lesion.

Methods Employed:

Liver biopsy samples from children with oligophrenia phenylpyruvica, as well as from normal controls from the same age group will be tested for the conversion of phenylalanine to tyrosine (see Project M - CP 6 for details).

Major Findings:

The assay system previously used for the work on animal tissues has been modified so that it is applicable to small (about 1 g.)
amounts of liver tissue. High activity has been obtained with 2 normal human liver samples. It has been possible to show that the cofactor, isolated from rat liver (see Project M - CP 8) can stimulate the human liver system 3-6 fold.

Significance to Mental Health Research:

A precise delineation of the metabolic block in this disease may help our understanding of the relationship if the metabolism of phenylalanine and tyrosine to normal brain development and function.

Proposed Course of Project:

Several additional normal samples of human liver will be checked for activity and then the studies on the oligophrenic liver samples will be carried out.

Part B included Yes /✓/ No /✗/
A.

**Project Title:** Biosynthesis of Noradrenalin

**Principal Investigator:** Bruce Levenberg, Ph.D.

**Man Years**
- Total: 1/3
- Professional: 1/3
- Other: -

**Project Description:**

**Objectives:**

This investigation is concerned with the mode of biosynthesis of the suprarenal hormone, noradrenalin. Evidence from tracer studies has indicated that a possible pathway of formation of this substance is from dihydroxyphenylalanine (DOPA) via hydroxytyramine (DOPA-amine). Research will be directed toward obtaining enzymatic evidence for such a series of reactions in cell free preparations of adrenal tissue. It will be of particular interest to make a detailed study of the postulated hydroxylation step between DOPA-amine and noradrenalin and to ascertain the nature of the enzymatic and cofactor requirements of such a system.

**Methods Employed:**

A simple and rapid chemical method has been devised for the estimation of small quantities of noradrenalin in tissue extracts in the presence of considerably larger amounts of DOPA-amine. Other methods are being perfected which will enable one to follow the course of the conversion of trace amounts of isotopically-labeled DOPA to noradrenalin in crude as well as in more purified enzyme preparations.

**Major Findings:**

Much of the time devoted to this investigation during the past several weeks has been spent on development of routine and reliable methods of assay. Thus, no major biochemical findings can be reported at this time.
Significance to Mental Health Research:

Adrenalin and noradrenalin, the major suprarenal medullary sympathomimetic agents, have been detected in considerable quantities in brain as well as in all types of adrenergic nerve tissue. The physiological and pharmacological actions of these hormones have become the subject of an almost overwhelming number of studies, but surprisingly little has been definitely established regarding the enzymatic mechanisms which the body employs in the biogenesis of the catechol amines from tyrosine. Much in the way of interest biochemical reactions lies therein, and it is hoped that information gained from this investigation will make a contribution in that direction.

Proposed Course of Research:

Since this is a new project, it is difficult to chart its course until specific findings are made. However, should the hydroxylase step be successfully demonstrated, purification of the enzyme components and a study of the intimate mechanism of the reaction are planned.

Part B included Yes /✓/ No /✗/
Project Title:  Sulfate Metabolism in Chlorella

Principal Investigator:  Graham A. Jamieson, Ph.D.

Years
Total:  1/2
Professional:  1/2
Other:  -

Project Description:

Objectives:

It has been suggested (Schiff, Thesis, Pennsylvania, 1956) that in the sulfur metabolism of Chlorella pyrenoidosa active methionine is formed without the intermediation of methionine. It was necessary to confirm these results (i) since the activation of methionine is the only known mechanism for the formation of active methionine, and (ii) as an attempt to clarify the role of the adenosine-homocysteine con- denzing enzyme isolated from rat liver since adenosyl homocysteine was a possible intermediate.

Methods Employed:

After the addition of carrier, active methionine was isolated by paper electrophoresis and chromatography from Chlorella cells which had been incubated with S35-sulfate and methyl-C14-methionine, respectively, of equal specific activity and the radioactivity of the product determined.

Major Findings:

It has been found that methionine is incorporated into active methionine by Chlorella eight to ten times more effectively than is sulfate suggesting that the pathway in this species is substantially similar to that in yeast and in the rat. A possible explanation for Schiff's erroneous results lies in the fact that the specific activities of his substrates were not carefully controlled and hence an apparent
non-incorporation of methionine as shown by radioautography was actually a dilution effect when compared with carrier-free sulfate.

Significance to Mental Health Research:

The importance ofonium compounds and of methyl transfer reaction in the metabolism of nerve tissue is well known. Because of the unusual mode of active methionine formation postulated by Schiff, it was imperative to clarify these findings in the hope of revealing new interrelationships between thioether and sulfonium compounds in order of understanding the biochemical basis of methyl group transfer.

Proposed Course of Research:

In view of our negative findings this project will not be continued.

Part B included Yes /✓/  No /✗/
Project Title: The enzymatic mechanism of generation of the methyl group of methionine from one carbon compounds such as formaldehyde.

Principal Investigators: Graham A. Jamieson, Ph.D., and Gabriel de la Haba, Ph.D.

Project Description:

Objectives:

To investigate the enzymatic mechanism of generation of the methyl group of methionine from formaldehyde. Recent investigations by other workers on the enzymatic reactions of formaldehyde or the beta carbon of serine, implicate a tetrahydrofolic complex such as a hydroxymethyl derivative as a metabolic intermediate. It is well known that formaldehyde, formate, or the beta carbon, of serine are converted to the methyl group of methionine (and that homocysteine is required for the generation of methionine from formate). The intimate details of this pathway, however, are unknown.

If a hydroxymethyl derivative of tetrahydrofolic acid is an intermediate, it is proposed that in a condensation with homocysteine--analogous to the reaction between adenosine and homocysteine described in Project No. M - CP 4 -- would result in a thioether, which upon subsequent reductive cleavage would yield methionine. Such a postulated mechanism is under investigation.

Methods Employed:

To facilitate the detection of the above postulated intermediate, radioactive formaldehyde and C14 carboxyl labelled homocysteine will be employed. To determine the extent of conversion of the formaldehyde to the methyl group of methionine the latter will be degraded to release specifically the methyl group as methyl iodide.
Part A. (Continued)

Major Findings:

This project is at the moment being initiated and as yet no results have been obtained. As a first step conditions for maximum reaction between tetrahydrofolic acid and formaldehyde were established and the complex isolated virtually free of formaldehyde.

Significance to Mental Health:

This project is part of the broad problem of methyl group transfer under investigation in this laboratory. For discussion of the significance to neurochemistry refer to a previous report (M - CP 4).

Part B included Yes / / No / /
Project Title: Amino acid uptake by *Escherichia coli*.

Principal Investigator: Michael Yarmolinsky

Man Years
Total: 2/3
Professional: 1/3
Other: 1/3

Project Description:

Objectives:

Determination of whether carboxyl activation is responsible for the concentration of amino acids by *E. coli*.

Methods Employed:

Amino acid uptake is measured by exposing suspensions of bacteria to radioactive amino acid and measuring the radioactivity of samples of bacteria separated from the medium by filtration.

Major Findings:

A specific, rapid, and reversible mechanism has been shown to be capable of concentrating methionine as well as its analogue ethionine in *E. coli*, strain W. The kinetics of uptake of the two amino acids are strikingly different.

Significance to Mental Health Research:

The mechanism of transfer of materials across cell membranes is of particular importance in nervous transmission as well as in the nutrition of all cells.

Proposed Course of Research:

It is expected to continue this project in the coming year.

B included Yes /✓/ No /✗/
Project Title: Amino acid incorporation and protein synthesis in liver.

Principal Investigator: Giulio L. Cantoni, M. D.

Years
- Total: 1-1/3
- Professional: 1/3
- Other: 1

Project Description:

Objectives:

The mechanism of biosynthesis of a protein de novo from its constituent amino acid is one of the most exciting problems presently under attack in biochemical laboratories throughout the world. While the structural complexity and fragility of proteins has so far made it impossible to attack the problem directly in a cell-free system in vitro, there are a number of less direct ways in which the problem can be approached. One line of attack which is of particular interest depends on the study of the uptake and incorporation of radioactive amino acid into proteins in a cell-free system.

Major Findings:

It has been established earlier that subcellular particles called microsomes are active in incorporating amino acids into proteins. It has now been found that different amino acids are incorporated at different rates with tryptophane being incorporated best and glycine least effectively. The kinetics, requirements and characteristics of the system are being investigated systematically. It is not known for certain whether amino acid incorporated by this system in fact enter into a peptide bond and the exact nature of the bond which binds the amino acid to the protein must be explored more directly.
Significance to Mental Health Research:

This project is of no immediate significance to mental health. However, inasmuch as the problem is a most basic one underlying our understanding of some of the most important facts in biology, it may be assumed that any progress toward its elucidation will be of potential interest to basic research in mental health.

Part B included    Yes /✓/   No /✗/
Project Title: Metabolism of "Active Methionine" in Yeast.

Principal Investigator: S. Harvey Mudd, M. D.

Yeast is known to synthesize and accumulate large amounts of S-adenosylmethionine ("active methionine") under certain nutritional conditions. Although this compound can serve as a donor of its methyl group or (after preliminary decarboxylation) of its aliphatic side chain, its metabolic fate in yeast remains to be elucidated and the goal of this project is to seek unknown reactions in which this compound may participate.

Methods and Findings:

Work is still in a preliminary stage. Chromatographic methods have been developed to enable ready separation and identification of micro and macro quantities of S-adenosylmethionine and related compounds. Very preliminary results suggest the possibility of a hitherto unknown reaction of S-adenosylmethionine catalyzed by a substance present in crude extracts of bakers' yeast.

Significance to Mental Health Research:

This project is part of a larger study on biological transmethylation the significance of which to mental health has been discussed elsewhere. It may be especially noted that the increasing evidence that a variety of methylated compounds of plant origin have powerful psychic effects suggests that any information on the metabolism of methyl compounds in plants may be of great significance for understanding both the natural and the therapeutic role of these substances.
Estimated Obligations for FY 1958

Total: $255,904
Direct: $245,975
Reimbursements: $9,929

Projects included: M-AR 1 through M-AR 6
Project Title: Addictive Liabilities of New Analgesics.

Principal Investigator: H. F. Fraser

Other Investigators: Harris Isbell

Cooperating Units: Laboratory of Chemistry, Section on Analgesics, NIAMD. The Office of Naval Research provided $33,835 in fiscal year 1957 and $33,385 in fiscal year 1958 to carry on investigations designed to find a synthetic substitute for codeine. This fund provided salaries for 5 subprofessional employees working five man years. NIMH Addiction Research Center provides administrative and supervisory services amounting to 1-1/3 man years.

Man Years (cal. yr. 1957): Patient Days (cal. yr. 1957):

Total: 6-1/3 4773 (not chargeable to Clinical Center)
Professional: 2/3
Other: 5-2/3
Project Description:

Objectives. To determine the addictive properties of new analgesic drugs as they are developed and prior to release for general sale. This is a technological program carried out in collaboration with the Drug Addiction Committee of the National Research Council and is designed to prevent uncontrolled use of potentially addicting drugs.

Methods Employed. Drugs are referred to the NIMH Addiction Research Center by the Committee on Drug Addiction and Narcotics of the National Research Council. The Addiction Research Center, using former addict volunteers, determines: (1) the psychological and physiological effects of single doses of the new drugs, (2) whether the new drugs will relieve or suppress symptoms of abstinence from morphine, and (3) in some cases, whether patients who are not tolerant to morphine can be directly addicted to the new drug.

Patient Material. No. Average Stay (days)
Admissions: 45 105
Outpatients: 56
No. of visits: 947

(Note: This patient material is not chargeable to the Clinical Center).

Major Findings. The following drugs were shown to have addictive properties:

1. d-1,2-Diphenyl-4-dimethylamino-3-methyl-2-propionoxybutane (d-propoxyphene),
2. Normorphine,
3. Norcodeine,
4. d-3-Methoxy-N-phenethylmorphinan.

The addictive properties of d-propoxyphene are so low (less than codeine) that the drug will not be controlled by the narcotic law. Normorphine is a slowly acting cumulative drug. Following withdrawal of normorphine, symptoms of abstinence are milder than after withdrawal of morphine.
Significance to Program of NIMH. Reports rendered to the National Research Council are the basis for recommendations concerning appropriate legal action connected with the control of these drugs at national and international levels. This prevents introduction of potentially addictive substance into uncontrolled use, thereby minimizing addiction to new drugs. We also hope to find a nonaddicting, pain-relieving drug, thus contributing further to the prevention of addiction. The psychological effects and mechanisms of action of these new drugs are frequently of great theoretical interest in the field of mental health.

Proposed Course of Project. Since this is a technological project operating for the protection of the public, it will be continued. Drugs tested will be those recommended by the National Research Council.
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:


4. Fraser, H. F., and Isbell, H.: Addiction Liability of New Analgesics:

   I. 1-(2-Morpholinethyl)-4-Phenyl-4-Carbethoxy-Piperidine (NIH-7299).

   II. 1-(2-Hydroxy-2-Phenethyl)-4-Phenyl-4-Carbethoxy-Piperidine (NIH-7292).

   III. 1-3-Methoxy-N-phenethylmorphinan (NIH-7362).

   IV. d-2,2-Diphenyl-3-Methyl-4-Morpholino-Butyl-Pyrroldine (NIH-7422).

Min. 18th Meet. Committee on Drug Addiction & Narcotics, NRC, Nat'l. Acad. Sci., 1957 (Mimeographed).
Part B: (continued)

Honors and Awards relating to this project:

Isbell, H.:  

1. Appointed Lecturer in Pharmacology with the Rank of Professor, University of Illinois, College of Medicine.

Part A.

Project Title: Acute and Chronic Intoxication with Drugs Other Than Analgesics, Barbiturates or Alcohol.

Principal Investigator: Harris Isbell

Other Investigators: A. Wikler

Cooperating Units: None

Man Years (cal. yr. 1957): 7
Patient Days (cal. yr. 1957): 636

Project Description:

Objectives. To determine the subjective and objective effects and pathologic physiology of drugs other than those in the opiate, barbiturate, and alcoholic classes. The drugs studied are of importance in that they: (1) may be abused by opiate addicts, (2) are reported to be of value in the treatment of addiction, (3) are reported to be of value in the treatment of mental disease, and (4) produce profound psychological effects. Examples of such agents are cocaine, mescaline, reserpine, and LSD.
Methods Employed. Appropriate doses of the drugs are administered acutely or chronically to former morphine addicts volunteers. Physiological, psychological, biochemical, and clinical measurements are made before, during, and after the intoxication.

Patient Material.

<table>
<thead>
<tr>
<th>No.</th>
<th>Average stay (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admissions: Adult Males</td>
<td>636</td>
</tr>
<tr>
<td>Outpatients</td>
<td>0</td>
</tr>
</tbody>
</table>

Major Findings. D-2-Brom-lysergic acid diethylamide (BOL), though far less potent than LSD, does have psychosomimetic properties when given in sufficient dose (4-8 mg./70 Kg.). Pretreatment of patients with BOL, BAS, and phenoxybenzamine did not attenuate or accentuate the LSD reaction. Administration of 0.4-0.6 mg. epinephrine at the height of the LSD reaction caused neither accentuation nor blocking of the LSD reaction. The following congeners of LSD all had psychosomimetic properties, but were less potent than LSD: \( \text{d-1-Methyl-lysergic acid diethylamide (MLD)}, \) \( \text{d-lysergic acid morpholide (LSM)}, \) \( \text{d-lysergic acid pyrrolidid (LPD)}, \) \( \text{d-lysergic acid dimethylamide (DAM)}, \) and \( \text{d-lysergic acid oxazolidone (LOC)}. \) \( \text{D-1-acetyl-lysergic acid diethylamide was as potent as LSD.} \)

Significance to Program of NIH. The psychosomimetic drugs provide means of safely inducing psychotic states in human volunteers. Various metabolic and toxic theories of the etiology of natural psychoses have been based on the effects of these drugs. Interactions of the psychosomimetic agents with tranquilizers, hormones, sympathomimetic blocking agents, etc., represent one way of testing these hypotheses.

Proposed Course of Project. This project will be continued with emphasis on interactions of LSD with neurohumoral blocking agents. A number of indole derivatives will be studied to determine if correlations exist between neurophysiological and pharmacological effects. As they become available, "toxins" isolated from blood and urine of schizophrenics will be studied.

Part B included: Yes [X] No [ ]
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:


Honors and awards relating to this project:

Isbell, H.:

Presented seminar, "Psychosomimetic Drugs," at University of Rochester School of Medicine, Rochester, New York, 23 October 1957.
Part A.

Project Title: Chronic Intoxication with Barbiturates and Alcohol.

Principal Investigator: H. F. Fraser

Other Investigators: Carl F. Essig

Cooperating Units: None

Man Years (cal. yr. 1957): 2-2/3

Patient Days (cal. yr. 1957):

- Total: 2-2/3
- Professional: -2/3
- Other: 2

Project Description:

Objectives. To determine clinical characteristics of intoxication with alcohol, barbiturates, and equivalent drugs; to determine minimal limits of dosage and time necessary for development of serious withdrawal symptoms; to study pathologic physiology of these intoxications; to develop more effective methods of treatment and prevention.
**Methods Employed.** Patients who have been chronically intoxicated with these drugs are stabilized on some predetermined dosage level; barbiturates or alcohol are then abruptly withdrawn or a drug presumed to be equivalent is substituted for the original drug; physiological, psychological, biochemical, and laboratory observations are made during both phases. Similar systems are used in animals.

<table>
<thead>
<tr>
<th>Patient Material</th>
<th>No.</th>
<th>Average Stay (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admissions:</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Outpatients:</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**Major Findings.** In sufficient dose alcohol suppresses abstinence from barbiturates in chronically intoxicated dogs almost completely. Following withdrawal of alcohol after substitution for barbiturates, dogs develop bizarre behavior and occasionally convulsions. These findings indicate partial equivalence of alcohol and barbiturates.

Following withdrawal of meprobamate after chronic intoxication with large doses, 3 of 4 dogs developed multiple convulsions and died in status epilepticus. The fourth dog survived although he had convulsions. These experiments definitely prove that meprobamate can produce physical dependence.

**Significance to Program of NIMH.** Alcoholism is a major mental health problem. Research in this field is therefore of great importance. The extensive use of barbiturates and of "tranquilizers" indicate that abuse of these drugs may have public health implications. It is very significant that one of the most widely used tranquilizers, meprobamate, has now been shown to be capable of producing addiction.

**Proposed Course of Project.** Equivalence of intoxications with barbiturates, alcohol, paraldehyde, chloral, and "tranquilizers" will be studied in dogs. Because of widespread use, first priority will be given to the tranquilizers. Treatments of delirium tremens will be studied, using dogs.

Part B included: Yes [X] No [ ]
Part B: Honors, Awards and Publications

Publications other than abstracts from this project:


Honors and awards relating to this project:

Fraser, H. F.:

Invited to participate in a Symposium on "Problems Resulting from Use of Habituating Drugs in Industry," Meeting of the American Public Health Association, Cleveland, Ohio, 14 November 1957.
Part A.

Project Title: Biochemistry of Addiction

Principal Investigator: A. J. Eisenman

Other Investigators: H. F. Fraser

Cooperating Units: None

Man Years (cal. yr. 1957): Patient Days (cal. yr. 1957):

Total: 3-2/3
Professional: 1-1/3
Other: 2-1/3

Project Description:

Objectives. To determine changes in chemistry in body fluids and organs arising from acute and chronic administration of drugs; determine rate, means of conjugation and destruction of drugs in body; study distribution of drugs in body; ascertain route and rate of excretion of drugs; and to determine effects of drugs on enzymatic processes.
Methods Employed. Standard methods of clinical, biochemical and chemical pharmacology are adapted to the special requirements of the individual experiments. Measurements of concentrations of drugs, their metabolites, and of various natural compounds in body fluids are made before, during, and after acute or chronic administration of drugs.

Major Findings. Chlorpromazine caused a diminution, and reserpine caused an increase in excretion of 17-hydroxycorticoids. Morphine and barbiturate addiction and withdrawal had inconsistent effects on the excretion of 5-hydroxy-indoleacetic acid. Addiction to and withdrawal of normorphine had effects on excretion of 17-hydroxycorticoids similar to those of morphine. A method for determination of normorphine was devised. Preliminary results indicate that not as much normorphine is conjugated as is morphine. This finding may explain the cumulative effect and mild degree of dependence on normorphine.

Significance to Program of NIH. Understanding of effects of drugs on chemical processes in the body is basic to understanding of the subjective effects produced by these drugs and, hence, to understanding of addiction. Differences in distribution, metabolism, and excretion may account for many of the differences in addictiveness of the various drugs.

Proposed Course of the Project. Studies on distribution, metabolism and excretion of normorphine as compared with morphine will be continued. Specificity of the normorphine method will be studied, and, if possible, an alternative method developed. As time permits, other demethylated analgesics will be examined. In order to study the role of the central and peripheral autonomic systems, studies on production, tissue levels, and excretion of epinephrine and nor-epinephrine will be undertaken during cycles of addiction.

It is also hoped that studies on enzyme activity can be initiated.

Part B included Yes [X] No [-]
Part A.

Project Title: Neurophysiology and Neuropharmacology of Addiction.

Principal Investigator: Carl F. Essig

Other Investigators: Harold G. Flanary, Abraham Wikler

Cooperating Units: None

Man Years (cal. yr. 1957): Patient Days (cal. yr. 1957):

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</table>

Project Description:

Objectives. To determine the effects of acute and chronic administration, as well as abrupt withdrawal, of addicting drugs upon the functioning of the central nervous system.

Methods Employed. In one chronic spinal dog, hindlimb reflexes were measured with standardized technics during chronic intoxication with 650 mg./day of sodium barbital for 5-1/2 months and after abrupt withdrawal of the drug. In cats, two studies were conducted: (a) the effects of chronic sodium
barbital intoxication (190 to 580 mg./day total for 180 days) upon the electroconvulsive threshold; for this study, a group of untreated cats was used as the control; and (b) the effects of cerebral electrical stimulation twice daily for four days prior to abrupt withdrawal of sodium barbital, after chronic intoxication as indicated above and continued thereafter during the abstinence period; for this study an unstimulated group of cats treated with sodium barbital in a similar manner was used as the control.

**Major Findings.** In the chronic spinal dog, abrupt withdrawal of sodium barbital was followed by the occurrence of three grand mal seizures, confined to the portion of the body innervated by the nervous system rostral to the level of spinal cord transection. In the lower limbs, the only definite change was a transitory disappearance of the extensor thrust reflex. In the cats, chronic intoxication with sodium barbital produces an elevation of the electroconvulsive threshold (for complete seizures); also, prewithdrawal and post-withdrawal cerebral electrical stimulation appears to reduce the incidence of withdrawal convulsions, but such stimulation is less effective if high doses of sodium barbital are used during chronic intoxication.

**Significance to Program of NIH.** Although, thus far, only one chronic spinal dog has been studied, the available evidence indicates that unlike morphine, physical dependence on barbiturates involves the rostral portion of the neuraxis more than the caudal. No final conclusion can yet be drawn from the studies in cats, but the available evidence suggests that seizures produced by electrical stimulation and those produced by withdrawal of barbiturate following a period of chronic intoxication share some more metabolic or physiological mechanisms in common.
**Proposed Course of Project.** All phases of this study will be continued along essentially the same lines, with the addition of electroencephalographic recording in the studies in cats. It is hoped that studies of biochemical systems responsible for synthesis and destruction of acetylcholine can be studied during the coming year. In addition, studies of effects of acute and chronic drug intoxication on activity of single neurons will be initiated.

Part B included Yes [X] No [ ]
Part B: Honors, Awards and Publications

Publications other than abstracts from this project:


Honors and awards relating to this project:

Wikler, A.: 

Appointed member of Behavioral Sciences Study Section, Division of Research Grants, NIMH.

Lectured on "Narcotics," Association for Research in Nervous and Mental Diseases, New York City, 13 December 1957.
Part A.

Project Title: Psychological Studies of Addiction.

Principal Investigator: Harris Hill

Other Investigators: A. Wikler, R. E. Belleville, and H. G. Flanary.

Cooperating Units: None

Man Years (cal. yr. 1957): Patient Days (cal. yr. 1957):

Total: 5-1/6
Professional: 2-2/3
Other: 2-1/2

Project Description:

Objectives. To determine psychological mechanisms of addiction, including relationships between personality characteristics and specific drug use; to measure intellectual, emotional, and psychomotor changes induced by acute and chronic intoxication with addicting drugs; to elucidate psychological mechanisms underlying pain relief by analgesic drugs.
Methods Employed. Standardized and new methods of clinical and experimental psychology are adapted to the above objectives. Clinical methods include standard psychometric and projective procedures, and development and use of original inventories. Experimental techniques involve measurements of perception, reaction time, contrived anxiety, and animal methods such as conditioning, experimental neurosis, etc. These methods are applied before, during, and after acute and chronic administration.

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Major Findings. Physician addicts comprised the only subgroup studied thus far which did not show marked psychopathic tendencies as measured by the Minnesota Multiphasic Personality Inventory. Although the average profile suggested neurotic tendencies and differed from that of normal men and medical students, it also differed very significantly from the profile of the "general" addict. Similar comparisons showed striking resemblance between Negro addicts and nonaddict Negro prisoners, and between White addicts, nonaddict White prisoners, and White alcoholics. Construction of questionnaire items which differentiated between CA-101, LSD-25, morphine, pentobarbital, and amphetamine in preliminary tests has completed the compilation of an inventory for distinguishing between drug effects. Continuing work on the proposed analgesic testing method in rats has increased the reliability of patterns of actions which differentiate the major classes of drugs. The potent analgesics produce nearly identical patterns of unconditioned bar pressing, "time-action" rates, and tone-shock conditioned inhibition of feeding responses.
Significance of Program to NIMH. The comparative studies on addicts and nonaddicts holds promise of providing some evidence on the significance of personality characteristics and availability of drugs in the addiction process. Efforts to measure "subjective" drug effects may produce techniques which will be differentially sensitive to analgesics, hypnotics, analeptics, psychotomimetics, and tranquilizers. The techniques may be useful in studying new addicting and nonaddicting agents, and may aid in developing a theory of drug actions. The animal technique may prove to be a reliable psychological procedure for screening potent analgesics. It may also provide a behavioral means of classifying drugs, and may aid in developing a theoretical frame of reference of drug actions.

Results of studies on mental set indicate that the LSD-syndrome is only indirectly related to the "natural" psychoses. Studies of effects of drugs on visual-hand reaction times as influenced by "regular" or "irregular" presentation of different warning ("foreperiods" or "setting periods"), using the procedure of Huston and Singer, showed the following: (1) after placebo, former addicts have faster reaction times than normal subjects, (2) morphine and pentobarbital slow reaction time but do not impair "mental set," (3) 1 mcg./kg. of LSD does not impair mental set in postaddicts (does not decrease the subjects' ability to profit from regular schedule of change of the "forewarning period," (4) 2-3 mcg./kg. of LSD reduces slightly the extent to which subjects profit from regularization of the presentation of the foreperiods, but the change is not significant despite pronounced distortions in perception, body image, hallucinations, etc., and (5) 20-40 mg. of amphetamine had little effect on reaction time or mental set.
Proposed Course of Project. During 1958, this section expects (1) to complete the study of physician addicts, and compare other groups of addicts and nonaddicts to further isolate the significance of personality characteristics and drug availability in the addiction process, (2) to further develop the inventory for measuring "subjective" drug effects by constructing preliminary scales through testing of subjects under various drugs, (3) to increase the reliability and validity of an analgesic screening technique in animals by investigating the effectiveness of different conditioned stimuli, (4) to investigate, by psychological methods, the significance of drug-produced internal changes in controlling animal behavior, and (5) to begin an animal study on the effects of drugs on discrimination.
Part B: Honors, Awards and Publications

Publications other than abstracts from this project:


Honors and awards relating to this project:

None
Basic Research
Laboratory of Clinical Science
Section on Cerebral Metabolism

BUDGET SHEET

Estimated Obligations for FY 1958

Total: $129,954
  Direct: $76,935
  Reimbursements: $53,019

Projects included: M-CS-CM 1 through M-CS-CM 7
Part A.

Project Title: Studies on the Circulation and Metabolism of the Human Brain. I. Age Changes in Cerebral Blood Flow and Metabolism. II. Effects of Anxiety and Emotional States on Cerebral Circulation and Metabolism.

Principal Investigator: Darab K. Dastur

Other Investigators: Louis Sokoloff, Seymour S. Kety, Douglas B. Hansen, Mark H. Lane

Cooperating Units: Section on Psychiatry, Laboratory of Clinical Science, NIMH, Serial No. M-CS-Ps(C)-1; Laboratory of Socio-Environmental Studies, NIMH, Serial No. M-S-D-4; Section on Aging, Laboratory of Psychology, NIMH, Serial No. M-P-A-3.

Man Years (calendar year 1957): Patient Days (calendar year 1957):

Total: 2.5
Professional: 1.0
Other: 1.5

Project Description:

Objectives: Numerous previous studies have demonstrated that with advancing age, cerebral blood flow and metabolic rate are reduced. Most of these studies, however, have failed to give evidence of any adequate control of the effects of various disease states often associated with aging. It is hoped in these studies to determine whether in the absence of any significant degree of age-related disease, these alleged reductions occur so as to ascertain whether they are representative of the process of aging per se within the central nervous system or dependent on disease. If they are still observed in carefully selected, relatively disease-free, elderly subjects, then it is hoped to determine whether the depressions of cerebral blood flow and oxygen consumption are secondary to circulatory deficiency and cerebral anoxia or a manifestation of primary changes within the central nervous system with concomitant readjustment of the cerebral
Project Description (Continued):

circulation. It is also hoped to investigate the possibility of correlations between changes in cerebral blood flow and metabolism with those occurring in various psychological and mental functions observed in old age.

Continuing efforts are being made to solve the question of whether the cerebral circulatory and metabolic functions are influenced by emotional factors and, if so, to determine the nature of such influences.

Methods Employed: The basic method employed in all these studies is the nitrous oxide method for the estimation of cerebral blood flow and metabolism in man.

Major Findings: Studies in over 50 normal elderly men carefully selected for their relative freedom from the common degenerative diseases of old age and who were functioning more or less normally in their homes and communities suggest that there are no reductions in cerebral blood flow and metabolic rate as a result of chronological age per se. The presence of hypertension in otherwise normal elderly men does not alter the picture. Chronic brain syndrome, on the other hand, is characterized by a reduction in metabolic rate of the brain. The results are too preliminary in this group to state whether there is evidence of primary circulatory deficit and cerebral anoxia or the reverse.

Concomitantly with the investigations in the aged, similar studies have been performed in normal young subjects so as to obtain adequate comparative control values. These young subjects as well as the aged have also been subjected to numerous psychological and psychiatric evaluations so as to determine the relationship, if any, among cerebral circulatory and metabolic functions on one hand, and psychological, psychiatric, mental, and personality factors on the other. Preliminary observations suggest that there may be such relationships.

Significance to Mental Health Research: All aspects of this project involve disturbances in mental or emotional functions whether arising from emotional disturbances or the degenerative processes of aging, or else are directed at learning more of the basic physiological mechanisms which determine the normal functioning of the cerebral circulation and metabolism. Since the brain is presumed to be the organ most intimately related to mental and emotional functions, studies of its circulation and metabolism in these conditions or in its normal state are directly pertinent to problems of mental health.
Project Description (continued):

Proposed Course of Project: Studies in normal old people will be expanded to include aged patients suffering from the psychoses of senility. Observations directed at uncovering any correlations between changes in cerebral blood flow and metabolism and alterations in psychological and mental functions will be made.

Part B included: Yes
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:


Other publications from previous work on this project:


Honors and awards relating to this project: None
Part A.

Project Title: Rapid Continuous Measurement of Leg Blood Flow and Metabolism by Means of Radioactive Sodium

Principal Investigator: Louis Sokoloff

Other Investigators: Mark Lane, Darab K. Dastur, and Douglas B. Hansen

Cooperating Units: None

Man Years (calendar year 1957): Patient Days (calendar year 1957):

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Project Description:

Objectives: The objective of this project is the development of a method for the rapid, continuous measurement of blood flow and metabolism in a region of the body of special interest to neurological research, the leg, and its application to studies in a variety of conditions in which these functions may be changing rapidly.

Methods Employed: The method employed is a newly developed method based upon the Fick Principle utilizing Na\textsuperscript{24} as the tracer material. The quantity of Na\textsuperscript{24} in the leg and its concentrations in the arterial and femoral venous blood are continuously monitored by means of scintillation counters following a rapid, single injection of Na\textsuperscript{24}Cl into the femoral artery of the experimental leg.

Major Findings: The development of the leg blood flow method has been satisfactorily completed. It has been employed in normal subjects at rest and during mild exercise and has been found to yield results almost identical with those obtained with other methods for measuring limb blood flow. It has likewise proved successful in measuring the leg blood flow continuously over minute-by-minute intervals for twenty to thirty minutes, and demonstrates the changes
Project Description (continued):

produced by mild exercise as well as vasodilator drugs such as priscoline, Arlidin®, etc. Studies in muscular dystrophy have shown that at rest, leg blood flow and oxygen consumption are markedly lower than normal, but they can be raised to normal levels during mild exercise.

Significance to Mental Health Research: The availability of a method for measuring leg blood flow and metabolism is of interest and usefulness for studies in neuromuscular diseases since by far most of the leg oxygen consumption is that of the muscles in the leg. Application of this in vivo method to studies of diseases such as muscular dystrophy may, therefore, shed light on some of the underlying disturbances in muscle metabolism presumed to exist in these diseases.

Proposed Course of Project: The initial phases of this project have been completed. The method for the rapid continuous measurement of leg blood flow and metabolism has been developed, and it has been applied to normal subjects at rest and during exercise, to studies of muscular dystrophy and to the testing of the efficacy and the determination of the continuous pattern of action of two reputed vasodilator drugs, Priscoline® and Arlidin®, following their intra-arterial injection. For the time being, no further experimental work is contemplated. The results of the work thus far will, however, be organized and definitely presented in three proposed publications.

Part B included: No
Part A.

Project Title: Measurement of Local Circulation in the Brain

Principal Investigator: Douglas B. Hansen

Other Investigators: Louis Sokoloff, Walter Freygang

Cooperating Units: Section on General Neurophysiology, Laboratory of Neurophysiology, NIMH, Serial No. M-NP-GN-1.

Man Years (calendar year 1957): Patient Days (calendar year 1957):

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Project Description:

Objectives: The application of a newly developed technique for the estimation of the blood flow through the various parts of the brain to physiological and pharmacological investigations directed at elucidating the various factors involved in regulating the normal regulation of the local cerebral blood flow or causing its alteration in pathological states.

Methods Employed: The method employed is one previously developed during the course of this project. It is based upon a theoretically derived mathematical expression which relates the tissue concentration of a freely diffusible inert substance to the history of its concentration in arterial blood, its solubility in the tissue, and the capillary blood flow per unit weight of tissue. By using a radioactive inert gas (trifluoriodomethane), the arterial concentration is recorded continuously by means of an appropriately designed scintillation counter, and by autoradiography, the concentration in the tissue is determined. From these data and the theoretical equation, capillary blood flow is calculated.
Project Description (continued):

Major Findings: Experiments in large numbers of cats have demonstrated the validity of the method for determining regional cerebral blood flow in 28 structures of the brain and spinal cord, and its ability to demonstrate changes in the local cerebral blood flow attending alterations in physiological and pharmacological states has similarly been proved. Normal values in blood flow per unit weight of brain tissue have been established in 28 structures of the conscious cat brain, and studies of the effects of pentothal anesthesia have demonstrated marked reductions in blood flow in those areas of the cerebral cortex chiefly concerned with primary sensory functions and which during consciousness, have, except for the inferior colliculus, the highest rates of blood flow in the brain. Retinal stimulation in unanesthetized cats by means of repetitive, high intensity photosflashes has been found to result in increases in blood flow in those areas of the brain involved in visual functions, for example, the visual cortex, the lateral geniculate ganglia, and the superior colliculi, provided the stimulation was maintained for five minutes. One-minute stimulation failed to produce any significant effect. These findings prove the adjustment of the local cerebral blood flow to local functional activity, and the latency of the adjustment suggests strongly that the mechanism is a chemical one probably related to the accumulation of the products of an increased metabolic rate. The sensitivity of the 28 brain structures to high and low oxygen tensions and high carbon dioxide tension have been studied. There does not seem to be differential effects on various structures, but white matter tends to change its circulatory rate less than gray matter.

Significance to Mental Health Research: The circulation of the brain is fundamental to a proper functioning of that organ, and disturbances in the cerebral circulation are known to be the basis of important neurological disorders and conceivably might play a roll in many neuropsychiatric disorders of unknown etiology. Since the brain is not a homogeneous organ, but is composed of a number of structures whose circulations might behave differently, measurement of the local cerebral blood flow could lead to a better understanding of normal and abnormal brain function and a means for evaluating various drugs and other types of therapy. Furthermore, the demonstration of the relationship between local cerebral blood flow and local functional activity indicates that the technique can be employed in the very basic purpose of mapping functionally related areas within the brain, knowledge of which could ultimately contribute to neurological diagnosis and therapy.
Project Description (continued):

Proposed Course of Project: In view of the apparent relationship between local cerebral blood flow and functional activity as demonstrated in the studies of visual stimulation, it is planned to evaluate the technique as a possible means of elucidating functional relationship between various brain structures. To accomplish this, the results of stimulation of various cerebral structures on other cerebral structures as regards both local blood flow and evoked potentials will be determined. In addition the method will be applied to studies of the nervous control of the cerebral circulation, the effect of carotid ligation, the question of cerebral vasospasm, and the effect of drugs with important nervous effects or functions, such as epinephrine and its oxidation products, LSD-25, and serotonin.

Part B included: Yes
Part B:  Honors, Awards, and Publications

Publications other than abstracts from this project:


Honors and awards relating to this project: None
Part A.

Project Title: The Mechanism of Action of Thyroxine and its Relation to Cerebral Metabolism

Principal Investigator: Louis Sokoloff

Other Investigators: Seymour Kaufman

Cooperating Units: Laboratory of Cellular Pharmacology, NIMH; Serial No. M-CP-7.

Man Years (calendar year 1957): Patient Days (calendar year 1957):

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Project Description:

Objectives: The ultimate objective of this project is the determination of the unique features of cerebral metabolism which render the mature brain independent of the circulating blood level of thyroid hormone. An intermediate objective, and probably a necessary step in order to attain the ultimate objective, is the determination of the mechanism of the physiological action of the thyroid hormone. In pursuit of this intermediate objective, the role of thyroxine in the regulation of protein synthesis and turnover is under investigation.

Methods Employed: The effect of thyroxine on the rate of incorporation of a radioactive amino acid (DL-Leucine-1-Cl4) into protein is studied in a completely in vitro system containing an actively phosphorylating mitochondrial system and a microsomal enzyme system. The mitochondrial system supplies the energy and the microsomal system the enzymes necessary for the in vitro synthesis of proteins. It is assumed that the rate of incorporation of the radioactive amino acid into the proteins of the system is related to the rate of synthesis of new protein molecules.
Project Description (continued):

Major Findings: Previous studies in the course of this project have demonstrated that thyroxine does penetrate the blood-brain barrier so that the failure of the mature brain to respond to elevated blood thyroxine levels cannot be attributed to the blood-brain barrier. Preliminary results thus far indicate that thyroxine does influence the rate of protein synthesis as indicated by an accelerative effect on the in vitro incorporation of radioactive amino acids into proteins. These results, however, have been variable probably because of a number of undetermined physiological and biological factors which are involved in this process but have thus far not been adequately controlled. During the past year a systematic attempt has been made to determine these variables so as to control them better. This attempt has met with some success so that the application of its results combined with a progressive improvement in techniques has led to a considerable increase in the consistency of the occurrence of the thyroxine effects and the predictability of the behavior of the entire system. In other words, as a by-product of the investigation of the action thyroxine has on protein synthesis, considerable fundamental information is being uncovered as to the various factors and mechanisms involved in the incorporation of amino acids into protein.

Significance to Mental Health Research: A unique feature of cerebral metabolism is its apparent lack of response to high circulating levels of thyroid hormone. An understanding of the basis of this unique behavior may reveal information concerning the cerebral metabolism in both health and disease. These studies may also throw light on the fundamental mechanisms of action of the thyroid hormone.

Proposed Course of Project: It is planned to pursue this project along the following lines: 1) To learn more concerning the mechanisms of amino acid incorporation into protein in order to assess its relationship to protein synthesis in an in vitro system, and to investigate the possibility of obtaining conditions more favorable to a thyroxine effect. 2) To investigate the possibility of utilizing or developing other more suitable methods for studying protein synthesis in vitro. 3) To study the effects of thyroxine analogues which do not have a latent period of action on the amino acid incorporation into protein. 4) To perform similar
Project Description (Continued):

studies in less purified systems, such as tissue slices, or to add additional factors or other hormones as indicated to the system so as to avoid the possibility of missing essential co-factors on whose presence the hypothesized action of thyroxine may be dependent.

5) To study the action of thyroxine on the activation of amino acids, a process believed to occur prior to their incorporation into protein.

Part B included: No
Project Title: Chromatographic Studies in Intermediary Metabolism Related to Diseases of the Nervous System

Principal Investigator: Darab K. Dastur

Other Investigators: None

Cooperating Units: None

Man Years (calendar year 1957): Patient Days (calendar year 1957):

| Total: 0.75                   | 170 |
| Professional: 0.75            |
| Other: --                     |

Project Description:

Objectives: The over-all objective of the project was twofold: 1) the investigation of the patterns of amino acids and organic acids in conditions of neuropsychiatric interest wherein metabolic errors are known or suspected to occur, as in phenylketonuria, Wilson's Disease, and muscular dystrophy; and 2) the establishment of experimental situations, in animals or man, whereby pharmacological or physiological stress is applied and the metabolic pathways studied, as in administration of phenylacetic acid to rats or of labeled phenylalanine to rats and monkeys, and in sleep deprivation in humans.

Methods Employed: For the greater part, paper chromatographic techniques have been employed for the delineation of amino acids and organic acids (such as some of the Krebs' cycle intermediates and some of the phenolic derivatives) in blood, urine and many of the tissues. Occasionally, quantification has been attempted by spot-elution and subsequent titration.

When radioactive isotopes have been used, techniques employing liquid scintillation counting and radioautography have been utilized.
Project Description (continued):

Major Findings: 1. Phenylketonuria: Upon a regime of special phenylalanine-free diet, the abnormal free phenolic acids seemed to disappear from the urines in phenylketonuric children observed for 2-3 months. There was concurrent reduction in phenylalanine excretion also. The level of phenylacetyl glutamine, more than normal in the pretreatment phase, diminished with the phenylalanine-free diet, and then increased a little again as normal articles of food were added to the diet. Whenever the initial hippuric acid level was also raised, it appeared to fall after the special diet.

2. Effects of phenylacetic acid: As this metabolite has been suspected to be toxic, it was administered intraperitoneally in large doses to rats one-month and six-months old, for periods up to six months. No striking change could be discerned in the condition of any of the animals. Regular urine examinations revealed the presence of large amounts of free phenylacetic acid, and an increase in the excretion of hippuric and phenaceturic acids. (All rats, including control animals who received injections of distilled H₂O, appeared to excrete much more aconitic acid than men or monkeys.)

In none of the rats have any of the tissues examined (blood, brain, liver, spleen, kidney, intestines, muscle, testis) ever shown any phenylacetic or hippuric or phenaceturic acid. Phenylacetic acid appears to be completely detoxicated and to be unable to pass the blood-brain barrier. Large amounts of acetyl aspartic acid were detected in all the brains.

3. Experiments with C₁₄-phenylalanine: Following intraperitoneal injections of uniformly labeled phenylalanine into rats, metabolic studies extending over 24 to 48 hours permitted almost complete "recovery" of the radioactivity, about three-fourths being from the tissues (especially muscles, intestines and liver). The rest was mostly expired as CO₂, only 3 per cent being excreted in the urine.

Following intravenous injection in the monkey, relatively less came out in the expired air, and about 20 per cent was still retained in the body at the end of five weeks (most within the liver).
Project Description (continued):

In radioautographs of chromatograms, radioactivity was detected in spots of phenylalanine, tyrosine, urea and hippuric acid in urines of both monkey and rat, and in phenylacetic acid, phenylacetyl glutamine, and succinic acid in the monkey. (In the course of the first eight hours, the monkey showed increased excretion of succinic and malic acids, together with glutamine and glutamic acid.) Acetyl aspartic acid was again conspicuous in the brain.

4. Wilson's Disease: Apart from a generalized aminoaciduria, varying with the severity of the neurological disorder, the only other feature of interest in the urines of the four subjects studied is a suggestion of increase in phenylacetyl glutamine.

5. Sleep deprivation: Urine samples from volunteers subjected to sleep deprivation for 60 to 70 hours were collected just before they were allowed to sleep, control samples being obtained from them three days later. Many of the subjects showed a clear increase of pyrrolidone carboxylic acid in the urine, while others did not manifest this feature. This was at times associated with prominence of glutamic acid also. Some revealed increased excretion of hippuric acid. Some of the group who received benzedrine sulphate during a second period of sleep deprivation, failed to show the increase in pyrrolidone carboxylic acid noted during the first study.

6. Lactic acid in muscle dystrophy: Samples of femoral venous blood from patients with muscular dystrophy obtained before and after exercise appeared to reveal in more than one-half the cases more lactic acid in the resting stage than after mild muscular exercise, this being most noticeable in the most severely dystrophic subject. In the other two cases, the picture was comparable to that obtained in normal subjects in whom there was no appreciable difference (as detected visually on the chromatograms) between the pre- and post-exercise periods.

Significance to Mental Health Research: Studies of the intermediary metabolism in diseases or abnormal states of function of the central nervous system may lead to basic information concerning the fundamental and specific biochemical processes of the nervous system.
Project Description (continued):

as well as to the uncovering of possible biochemical defects in such disorders.

**Proposed Course of Project:** For the time being, it is intended to analyze further the data collected, complete some of the quantitative studies and prepare some of the data for publication.

**Part B included:** No
Part A.

Project Title: Determination of the Spinal Fluid Levels of \( \gamma \)-Aminobutyric Acid and the Enzyme Responsible for its Formation, Glutamic Decarboxylase, in Normal Subjects and in Patients with Mental and Neurological Disease

Principal Investigator: Thomas Vates

Other Investigators: Louis Sokoloff, Bernard Agranoff

Cooperating Units: Section on Lipid Metabolism, Laboratory of Neurochemistry, NINDB.

Man Years (calendar year 1957): Patient Days (calendar year 1957): 70

Total: 0.1
Professional: 0.1
Other: --

Project Description:

Objectives: Recent developments in neurochemistry and neurophysiology indicate that \( \gamma \)-aminobutyric acid may be, if not itself, closely related to one of the chemical mediators of central nervous system inhibition. It is formed from glutamic acid by an enzyme, glutamic decarboxylase, which apparently is distributed uniquely only within the nervous system. It is the purpose of this project to develop methods for the assay of both the enzyme and its product in the spinal fluid of normal subjects and in diseased patients in whom alterations in their levels may reasonably be suspected. The patients will include schizophrenic patients, particularly of the catatonic type, and patients with neurological diseases in which there may be active brain damage. If feasible, it is planned to develop the technique to a point of clinical usefulness as a test for the presence of active brain damage in much the same way as serum transaminase levels have been employed for myocardial damage.
Project Description (continued):

Methods Employed: Glutamic decarboxylase concentration will be determined from its influence on the rate of release of $^{14}$O$_2$ from saturating amounts of $^{14}$-glutamate under optimal conditions for the activity of this enzyme. $^{14}$O$_2$ will be trapped in strong alkali and measured in a liquid scintillation counter. $\gamma$-Aminobutyric acid will be determined by a fluorometric method.

Major Findings: Preliminary studies have demonstrated that there are measurable amounts of active glutamic decarboxylase in the cerebrospinal fluid and that the proposed methods will be adequate to assay them.

Significance to Mental Health Research: In view of the possibility that $\gamma$-aminobutyric acid may be involved in central nervous inhibition, the determination of its level in spinal fluid may provide a means of approaching in human beings the detection of abnormalities in this function. It is conceivable that such abnormalities may occur in diseases such as catatonic schizophrenia in view of the clinical symptomatology. Also, the enzyme, glutamic decarboxylase, appears to be specifically located in the central nervous system, and during active damage of the nervous tissues, may leak into the spinal fluid in significant amounts. The assay of its level may then become a very useful clinical tool in neurology for diagnosis and prognosis regarding the degree of active damage of nervous tissues, from which some recovery or progression may occur, as contrasted with permanent, but not active or progressive, functional impairment.

Proposed Course of Project: The initial phase of the project will be directed at refining the techniques to the point of obtaining trustworthy quantitative results. Normal values for both the enzyme and the $\gamma$-aminobutyric acid will be determined. Simultaneously, comparative values will be obtained in patients with schizophrenia, cerebral palsy, cerebrovascular accident, and other nervous and mental diseases.

Part B included: No
Part A.

Project Title: Copper Dynamics in Normal and Schizophrenic Serum

Principal Investigator: Douglas B. Hansen

Other Investigators: Seymour S. Kety

Cooperating Units: None

Man Years (calendar year 1957): Patient Days (calendar year 1957):

Total: 0.25  72
Professional: 0.25
Other: --

Project Description:

Objectives: To study the fate of radioactive copper within the blood serum of normal and schizophrenic man.

Methods Employed: After intravenous injection of copper-64 into normal volunteers and schizophrenic patients, blood is removed at varying intervals and the serum protein analyzed by electrophoresis. The various protein fractions are separated and the radioactivity determined by appropriate scintillation counter technique in the different fractions.

Major Findings: Preliminary cat experiments have been done and the technique worked through, the approximate quantity of radioactivity needed has been determined, and the findings that copper is initially bound to albumin and gradually transfers to the $\alpha_2$ fraction, which contains the ceruloplasmin, has been confirmed.

Significance to Mental Health Research: One of the current theories of the etiology of schizophrenia is based upon the controversial finding of some investigators that the copper-containing protein (ceruloplasmin) in the blood of schizophrenics is altered either in quantity or character
Project Description (continued):

from normal. Such a study as proposed here would study in vivo the dynamics of the major characteristic of this protein, i.e. the bound copper.

Proposed Course of Project: To see if the transfer of copper into and out of the ceruloplasmin molecule is altered in selected and diet controlled schizophrenic patients from normal volunteers. A positive result would be the occasion of further investigation into the characteristics of the protein.

Part B included: No
Estimated Obligations for FY 1958

Total: $64,879
Direct: $49,849
Reimbursements: $15,030

Project included: M-CS-DE 1
1. Laboratory of Clinical Science
2. Section on Drug Evaluation
3. St. Elizabeths Hospital, Washington, D. C.

PHS-NIH
Individual Project Report
Calendar Year 1957

Part A.

Project Title: Determination of Cerebral Blood Flow and Metabolism in Brain Disease by Means of the Inert Gas Technique Utilizing Krypton 85.

Principal Investigators: Mark H. Lane, Niels A. Lassen

Other Investigators: Irwin Feinberg, Louis Sokoloff, Seymour S. Kety

Cooperating Units: St. Elizabeths Hospital, Washington, D. C.

Man Years (calendar year 1957): Patient Days (calendar year 1957):

<table>
<thead>
<tr>
<th>Total:</th>
<th>1.75</th>
</tr>
</thead>
<tbody>
<tr>
<td>Professional:</td>
<td>1.25</td>
</tr>
<tr>
<td>Other:</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Project Description:

Objectives: To make measurements of cerebral blood flow and metabolism in brain disease by use of the inert gas technique, utilizing Krypton 85, a radioisotope, as the inert gas. By this method it is possible to obtain more accurate definition of the uptake of the gas by the brain, especially in the early, more rapid uptake phase. By making bilateral simultaneous determinations, the questions of side-to-side differences are also being investigated. Thus, by these techniques it is hoped to answer the following questions: 1) the age at which a reduction in cerebral oxygen metabolism is demonstrable in normal man; 2) do psychological signs of decreased mental function correlate with reduction in cerebral oxygen metabolism; and 3) are the curves of cerebral inert gas uptake resolvable into components which are physiologically meaningful?

Methods Employed: The method of cerebral blood flow determination employed is essentially that of Kety and Schmidt that has been used at the NIMH for the last three years, with two modifications. First, cerebral venous blood is sampled from both internal jugular veins.
simultaneously, and secondly, the radioactive inert gas, Krypton 85, is used instead of nitrous oxide. As far as is known this is the first use of Krypton 85 for cerebral blood flow determinations in this country.

Patient Material: Up to the present time this technique has been performed on four young normal control subjects at the NIH and two patients with arteriosclerotic senile brain disease at St. Elizabeths Hospital. It is anticipated that many more brain disease patients will be studied as well as a few normal control subjects to establish normal values of blood flow and metabolism for the St. Elizabeths Hospital laboratory.

Major Findings: Since this project has just barely begun, there are no major findings to report as yet. From the preliminary studies completed the technique appears promising.

Significance to Mental Health Research: As the brain is recognized as the organ of the mind, a study of the physiology of brain metabolism and circulation as related to mental processes is desirable. Bilateral determinations of the cerebral blood flow and the metabolic rate of oxygen are thought to be less variable among individuals and more reproducible than unilateral studies, particularly with the use of Krypton 85 as the inert gas. Strong relationships established between psychological deficit and whole brain circulation and metabolism measured by an accurate, reproducible method would open broad avenues of research in diagnosis and in the evaluation of treatment of brain disease.

Proposed Course of Project: This project at St. Elizabeths Hospital was first proposed in February 1957. Over the next months, equipment was ordered, special equipment constructed and surplus material from NIH salvaged for use in the new laboratory. An extensive application for the use of Krypton 85 at St. Elizabeths Hospital was prepared for the Atomic Energy Commission, and the project submitted to the Radioisotope Committee of NIH and a newly formed committee at St. Elizabeths Hospital. The project was submitted to the Research Committees of both institutions. Temporary laboratory space at St. Elizabeths Hospital was negotiated for and the area modified for laboratory use. Equipment was installed, instruments tested and analytical procedures were standardized for the new laboratory by November. A
Project Description (continued):

biophysicist and radiation safety officer was obtained for the St. Elizabeths Hospital laboratories. Patients were screened for suitable subjects, psychiatrically and medically. Final approvals by all committees and agencies were obtained by the first week in November. Four preliminary studies were performed at the NIH during the summer. The first bilateral cerebral blood flow measurement utilizing Krypton 85 at St. Elizabeths Hospital was performed on November 7, 1957. It is desired that by the end of June 1958 a group of at least 25 to 30 organic brain disease patients will have been studied, with at least one repeat determination on each subject. A similar group of normal young and old subjects and functionally psychotic patients are to be studied as controls, as available.

Part B included: No
NATIONAL INSTITUTE OF MENTAL HEALTH

Basic Research
Laboratory of Clinical Science
Section on Biochemistry

BUDGET SHEET

Estimated Obligations for FY 1958

Total: $68,145
  Direct: $52,359
  Reimbursements: $15,786

Projects included: M-CS-B 1 through M-CS-B 5
Part A.

Project Title: Fractionation of brain constituents. Isolation and identification of antigen responsible for production of allergic encephalomyelitis.

Principal Investigator: Marian W. Kies

Other Investigators: Elizabeth Roboz, Ellsworth C. Alvord, Jr.

Cooperating Units: Georgetown University Medical School, Washington, D.C. and Baylor University Medical School, Houston, Texas.

Man Years (calendar year 1957): 1 1/3
Professional: 1/3
Other: 1

Patient Days (calendar year 1957): None

Project Description:

Objectives: The isolation and characterization of the material in brain responsible for the allergic demyelinating processes.

Methods employed: Brain and spinal cord preparations have been fractionated by classical biochemical procedures and the various fractions tested by injection in guinea pigs. The test has been refined so that it can be used as a bioassay for encephalitogenic activity. Each animal is assigned a disease index derived from clinical, histologic and serum lipid ratings, made independently by two observers. The disease index varies from 0 (no reaction) to 10 (maximum reaction). The average of 10 animals injected simultaneously is the disease index for any given weight of material. One unit of activity is defined as that amount eliciting an average D.I. of 4 (half maximal effect) in a group of 10 animals. Thus, for any given fraction, the specific activity (units/mg.) or total activity can be calculated and compared.
Part A. Project Description (continued)

with the starting material. Data from experiments on about a thousand animals were used to develop the disease index, and we feel that we have a valid reproducible method of assay. The standard error of the mean for each series is about ± one D.I. unit.

Major findings: ED50 values have been established for lyophilized guinea pig brain and bovine cord. Their activity is compared with the most active fractions yet obtained in the table:

<table>
<thead>
<tr>
<th>I. Bovine spinal cord</th>
<th>ED50*</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Collagen like protein (II-B)</td>
<td>0.025</td>
</tr>
<tr>
<td>B. 5% KCl xt. of CAP</td>
<td>0.005</td>
</tr>
<tr>
<td>C. Citrate xt., whole cord</td>
<td>0.007</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>II. Guinea pig brain</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>A. pH 3 xt. of defatted brain</td>
<td>0.006</td>
</tr>
</tbody>
</table>

* Weight of material eliciting a half-maximal response.

An accurate determination of the ED50 value for a given fraction requires a minimum of 20 animals. Usually more are required to determine the range in which the response is proportional to the dose.

The collagen-like protein (II-B) which was isolated from hot solvent extracted cord was found to be a single homogeneous protein by electrophoresis and ultracentrifugation. It contains hydroxy-proline and hydroxylysine and chemically is very similar to collagen from bone and skin.

Fractions B and C from whole cord (KCl and citrate extracts) are unheated, undenatured preparations, and since they are chemically similar, they may contain the same active constituent. They are distinctly different from the collagen-like protein in that they contain no detectable hydroxyproline or hydroxylysine.

Fraction II-B has been tested, at our request, in rabbits by Dr. B. Waksman and in mice by Dr. J. Lee. It appears that in neither species is this fraction active. On the other hand, the lipid soluble fraction which Folch and Lees have prepared possesses only minimal activity in guinea pigs. Its activity in rabbits is also of much lower magnitude than that of fresh whole cord. Dr. Waksman has already published these results, even though the experiment was presumably a
Part A. Project Description (continued)

collaborative one, as a proof of species specificity and multiplicity of antigens. The fact that the rabbit is so much less sensitive to whole nervous tissue than is the guinea pig makes us hesitant about accepting this explanation.

Significance to Mental Health Research: This investigation is basic to an understanding of the pathological process known as demyelination. Any organic brain damage, if sufficiently extensive, will lead to impaired mental processes.

Proposed course of project: (a) Further fractionation of the acid extract of defatted guinea pig brain material. (b) Dr. Roboz will continue her studies on the KCl extract of whole bovine cord. If both sources yield pure proteins, they will be characterized as completely as possible to see how they differ (if at all) in chemical composition. (c) Other investigators have agreed to test our protein fractions in rabbits and monkeys.

Part B included    Yes
Part B: Honors, Awards and Publications

Publications other than abstracts from this project:


Honors and Awards relating to this project:

One important professional contribution on this project was our help in arranging a Symposium on Experimental Allergic Encephalomyelitis and its Relation to other Diseases of Man and Animals. In June, 1956, Drs. E.C. Alvord, Jr., E. Roboz, P.Y. Paterson and I approached Dr. Gordon Seger about the possibility of a grant from the NINDB Advisory Council to support such a symposium. In November, 1956, they made available to us the sum of $5000 to hold a conference here at NIH. Drs. Alvord, Paterson, Roboz and Kies, with Dr. Henry Imus of NINDB constituted the committee on arrangements.

Subsequently, we were able to obtain an auxiliary grant from Smith Kline & French Research Foundation for $2500, to help defray the expenses of certain foreign investigators whom we wished to attend.

A two day conference was held on October 19 and 20, 1957. About 70 people attended, at least 50 of whom took a very active part in the discussion. The formal papers and pertinent discussion will be published in book form by Charles C. Thomas, Publishers, and will be edited by Drs. Alvord, Paterson and Kies.

The program was divided into three categories - pathology, etiology and immunology. Dr. Alvord was responsible for arranging the pathology program, Dr. Paterson for immunology, and the session dealing with etiology was my responsibility.

From the enthusiastic response during discussion periods and from personal comments of participants, both written and verbal, we are quite sure that the symposium was well received and served a most useful purpose.
Part A.

Project Title: Immunological studies on allergic encephalomyelitis.

Principal Investigator: Marian W. Kies

Other Investigators: Ellsworth C. Alvord, Jr.

Cooperating Units: Baylor University Medical School, Houston, Texas.

Man Years (calendar year 1957) Patient Days
Total: 1 1/3 (calendar year 1957)
Professional: 1/3
Other: 1

Project Description:

Objectives: Investigation of the immunological aspects of allergic encephalomyelitis in an attempt to obtain definitive evidence, pro or con, on the question of the allergic nature of the condition.

Methods employed: The standard assay technique described in another project report has been utilized to study the function of the tubercle bacillus in the production of allergic encephalomyelitis.

Major findings: (a) Protective action of the tubercle bacillus in mineral oil emulsion. If adult animals are injected with incomplete vaccine (tubercle bacilli and oil) 30 days before a complete vaccine (tubercle bacilli, oil and brain fraction) they can be completely protected against the encephalitogenic effect of the latter. This protective effect is inherent in the tubercle bacilli (oil alone is ineffective) but the protection afforded by tubercle bacilli is potentiated when it is given in an oily vehicle rather than saline. The protective action of 0.01 mg. tubercle bacilli in oil is almost as great as 0.25 mg. tubercle bacilli in saline.
Part A. Project Description (continued)

Contrary to the results reported by Dodd and Bigley, the guinea pigs receiving these low molecular weight carbohydrates showed no clinical signs of disease, were normal on histologic examination, and their serum electrophoretic patterns were completely normal. Total serum proteins, total polysaccharide and serum hexosamine contents were also within normal limits.

The discrepancy between their results with rabbits and ours with guinea pigs may be a species difference. However, they used such massive doses, that their results may have come from toxicity effects rather than an antigenic reaction.

It was important to check their observation, because of the (remote) possibility that the encephalitogenic effect of nerve tissue might be due to these or related carbohydrates.

Pursuing this same line of reasoning, a polysaccharide fraction isolated from brain by the method of Glegg and Pearce was tested in the same manner for encephalitogenic activity and for its effects on serum proteins.

No clinical, pathological nor biochemical effects were noted. This material which was obtained in 0.04% yield contained 2.7% of nitrogen, 10.8% hexose, 13.6% hexosamine, and 32.9% uronic acid. Chromatographic analysis of a hydrolyzed sample showed no detectable amino acids, but indicated the presence of the monosaccharides usually found in nerve tissue: galactose, mannose and fucose, and galacturonic acid. In addition, rhamnose was also found to be present. This methyl pentose which is related structurally to mannose, has never been reported in brain tissue, to our knowledge.

Two other fractions obtained by Glegg's procedure were probably glycoproteins, since their nitrogen content was much higher (7.7, 12.7%) and the total hexose lower (6.6 and 0.6%). Chromatographic analysis of their respective hydrolysates showed the amino acids and monosaccharides usually found in brain materials. These fractions were also inactive biologically. This protective effect can be elicited in new born guinea pigs i.e. the preliminary incomplete vaccine is given to day old guinea pigs and the subsequent complete vaccine at about 3 months (500 gm.). Interestingly, the new born guinea pig is not susceptible to the complete vaccine. No illness results when a day old guinea pig is injected with brain fraction and tubercle bacilli in oil. Therefore, different immunological mechanisms must be involved in the development of protection and the induction of the disease. The early belief that the reason the immature animal does not respond to the injection
of brain material is that he has not yet formed myelin is incorrect. The brain of the day old guinea pig is known to contain myelin and furthermore, brain tissue from day old guinea pigs can induce the disease in the adult animal.

(b) Degraded fragments of tubercle bacillus prepared by Dr. Colover of Taplow, England, have been tested in our laboratory and found to be active when combined with a purified protein fraction from cord. Whether or not their specific activity is comparable to whole tubercle bacillus cannot be determined until both the fractions and the whole bacillus have been tested at several levels. (See proposed course of project.)

Significance to mental health research: Although experimental encephalomyelitis is assumed to be an allergic manifestation by many investigators, it has never been definitely proven. The experiments in progress may not result in unequivocal evidence, but they should lend weight to one side of the argument.

This project offers a good possibility of determining the physiological conditions which predispose an individual to the development of spontaneous brain lesions and subsequent neurological and psychotic effects.

Proposed course of the project: Brain fractions found to be active in producing allergic encephalomyelitis will be used for skin sensitivity tests in guinea pigs. We would like to investigate the relation of delayed type skin sensitivity in the guinea pig to the disease process.

To our knowledge, no attempts to titrate the effectiveness of tubercle bacillus have been made except for some unpublished results of Dr. J. Freund, which are not complete. We are at present attempting to correlate the amount of tubercle bacillus required for maximum effect with the amount of brain injected. It may be that marked differences in susceptibility to lipid and protein antigens exhibited by rabbits, guinea pigs and mice may be related to varying requirements for tubercle bacillus with different antigens in different species.
Part A.

**Project Title:** Biochemical studies on brain, blood, and spinal fluid of encephalomyelitic animals.

**Principal Investigator:** Marian W. Kies

**Other Investigators:** Joseph B. Murphy and Ellsworth C. Alvord, Jr.

**Cooperating Units:** Baylor University Medical School, Houston, Texas.

**Man Years (calendar Year 1957)**  
Total: 2 1/3  
Professional: 1/3  
Other: 2

**Patient Days (calendar year 1957):** None

**Project Description:**

**Objectives:** To ascertain what biochemical changes occur prior or during the acute stage of allergic encephalomyelitis, in order to understand the basic mechanisms involved in the disease.

**Methods employed:** (a) Electrophoretic analysis of serum from normal and encephalitic animals. (b) Analysis of serum for total protein, total polysaccharide and hexosamine.

**Major findings:** Following a verbal report at the April, 1957 Federation Meetings, that injection (of massive doses) of \( \alpha \)-d-galacturonic acid and glucuronolactone in rabbits produced typical lesions of encyphalomyelitis, a similar test was made in guinea pigs, but with more reasonable amounts of "antigen". Because the authors of this report (Dodd and Bigley) had noted characteristic blood changes in their experimental animals, serum studies were also carried out.

From these results, we have concluded that the encephalitogenic activity found in whole brain tissue is not associated with carbohydrate per se, but requires a specific protein. It is interesting that all of the active protein fractions which
Part A. Project Description (continued)

have been prepared in our laboratory or by Dr. Roboz
have contained small amounts of nondialyzable carbohydrate.
(None have been found to contain rhamnose, however.)

Significance to Mental Health Research: Almost nothing
is known regarding the cause of spontaneous demyelinating
diseases in humans. This disease offers the best experi-
mental approach to their study at the present time.

Proposed course of project: (a) Extension of earlier studie
on the lipemia associated with allergic encephalomyelitis.
It is proposed to study the normal and abnormal lipoproteins
by preparative ultracentrifugation. (b) Electrophoretic
studies of brain proteins, especially the encephalitogenic
fractions obtained from chloroform-methanol extracted brain.
(c) A recent report on changes in α globulin patterns just
prior to the onset of symptoms in experimental allergic
encephalomyelitis has suggested we reinvestigate the serum
globulin pattern relative to the course of the disease.

Part B included  Yes
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:


Honors and Awards relating to this project: None.
Project Title: Antidiuretic effects of LSD in normal and schizophrenic subjects.

Principal Investigator: Marian W. Kies

Other Investigators: Edward V. Evarts

Cooperating Units: None

Man Years (calendar year 1957): Total: None  Patient Days (Calendar year 1957): None.

Professional: None

Other: None

Project Description:

Objectives: To study the responsiveness of the hypothalamus in normal and schizophrenic subjects under standard conditions of stress, and to develop methods for determining the level of antidiuretic substance in blood.

Methods employed: A study of urine output, pH, chlorides, and specific gravity under standard basal conditions and following the administration of a stress-producing drug such as lysergic acid diethylamide.

Major findings: No work had been done on this project this year. See Publications.

Significance to Mental Health Research: Although the site of action of LSD has not been established, there has been considerable speculation that some of the psychological effects are related to hypothalamic stimulation. Since the antidiuresis observed was similar in certain respects to the effect of increased production of ADH (a well known corollary of hypothalamic stimulation), the data are consistent with the notion that...
Part A. Project Description (continued)

Hypothalamic stimulation is related to the psychological effects of LSD.

Proposed course of project: We hope to do a companion experiment on mentally disturbed patients.

Part B included Yes
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:


Honors and Awards relating to this project: None.
Part A.

Project Title: Metabolism of radioactive histidine in Schizophrenics and normal humans.

Principal Investigator: Marian W. Kies

Other Investigators: Donald D. Brown

Cooperating Units: None.

Man Years (calendar year 1957): Patient Days
Total: (calendar year 1957): None
  Professional: Other: 1/4

Project Description:

Objectives: To study and compare the metabolism of the amino acid L-histidine in normal control humans and schizophrenics.

Methods employed: (a) Administration of uniformly labelled carbon-14 histidine. (b) Analysis of the urine for the metabolites using ion-exchange resins, paper chromatography and radioactivity determinations.

Major findings: Preliminary studies with the rat have been done to establish the biological half life of radioactive L-histidine. Urine and carbon dioxide were collected for two days, the animal sacrificed, and a variety of organs analyzed for carbon-14. About 30% of the injected radioactivity was excreted in the CO₂ and urine; the remainder was found in the tissues with the highest concentration in the liver.

At present a method is being devised to identify histidine metabolites in the urine. The use of ion-exchange resins has given encouraging preliminary results. It is hoped that enough initial information will be available soon to begin work with patients.
Part A. Project Description (continued)

Significance to mental health research: Studies on schizophrenic twins have indicated that the disease is genetically controlled. If susceptibility to schizophrenia is a genetic phenomenon, it should be possible to demonstrate some metabolic abnormality in people suffering from this disease. This project is one phase of a larger study on carefully chosen schizophrenics with presence or absence of familial incidence as the criteria of selection.

Proposed course of project: The animal studies described will be used as a guide for similar studies on human urine and blood. Metabolic studies on two classes of schizophrenics — those with a marked familial tendency to schizophrenia and those with no known familial tendency — and on normal controls of comparable ages will be made.

Histidine is one of several amino acids which will eventually be studied. It is interesting because it is the precursor of histamine, which has been claimed by certain investigators to be abnormally high in blood from schizophrenics.
NATIONAL INSTITUTE OF MENTAL HEALTH

Basic Research
Laboratory of Clinical Science
Section on Pharmacology

BUDGET SHEET

Estimated Obligations for FY 1958

Total: $53,231

Direct: $40,899

Reimbursements: $12,332

Projects included: M-CS-Ph 1 through M-CS-Ph 3
Part A.

Project Title: Biochemical factors involved in the action of drugs. I. Studies on the development of tolerance to narcotic drugs and the action of narcotic drug antagonists.

Principal Investigator: Julius Axelrod

Other Investigators: Joseph Cochin

Cooperating Units: Laboratory of Chemistry, Section on Analgesics, NIAMD, Serial No.

Man Years (calendar year 1957) Patient Days
Total: 1 1/3 (calendar year 1957): None
Professional: 1/3
Other: 1

Project Description:

Objectives: The phenomenon of tolerance to narcotic drugs has been the subject of numerous investigations, but no satisfactory explanation has thus far been evolved. For this reason, a study on the biochemical factors involved in the development of tolerance and the action of narcotic drug antagonists was undertaken.

Methods employed: General biochemical and pharmacological procedures.

Major findings: Previous studies have shown several striking similarities between receptors for narcotic drugs and the enzymes that N-demethylate these drugs. The enzymes and receptors have been found to be alike with respect to the type of substrates with which they interact, stereospecificity and antagonism by N-allylnormorphine.

An examination of the effect of the repeated administration of N-allylnormorphine, a narcotic drug antagonist, and normorphine, a drug with weak analgesic action, on the enzymatic demethylation of morphine and analgesic response
Part A. Project Description (continued)

was studied. The repeated administration of N-allylnormorphine resulted in the development of tolerance to morphine and a concommitent reduction in the enzymatic N-demethylation of morphine. Similar results were obtained after the repeated administration of normorphine. These findings further substantiate the mechanism of tolerance to narcotic drugs previously proposed.

Significance to Mental Health Research: It is hoped that information obtained from these investigations may give some insight into the phenomenon of tolerance, cross tolerance and antagonism to narcotic drugs.

Proposed course of project: The effect of sex hormones on the N-demethylating enzyme and response to morphine in morphine treated animals will be examined. The effect of the repeated administration of drugs which produce tolerance (e.g. LSD, barbiturates) on the enzyme systems which metabolize these drugs will be studied.

Part B included Yes
Part B: Honors, Awards and Publications

Publications other than abstracts from this project:


Honors and Awards relating to this project:

Invited to deliver lecture on the mechanism of tolerance to narcotic drugs, to Lilly Research Laboratories and Howard University.
Part A.

Project Title: The Physiological Disposition and Metabolic Fate of Drugs Affecting the Nervous System.

Principal Investigator: Julius Axelrod

Other Investigators: Bernhard Witkop and Bernard Agranoff

Cooperating Units: Laboratory of Chemistry, NIAMD, Serial No. , Section of Lipid Metabolism, Laboratory of Neurochemistry, NINDB, Serial No.

Man Years (calendar year 1957): Patient Days
Total: 5/6 (calendar year 1957): None
Professional: 1/3
Other: 1/2

Project Description:

Objectives: This project is concerned with the absorption, excretion, plasma levels, rate of biotransformation tissue distribution, and metabolic pathways of drugs acting on the nervous system. Drugs under study at present are epinephrine and norepinephrine, metanephrine and normetanephrine and meprobamate.

Methods employed: Biochemical and pharmacological procedures.

Major findings: A method for the estimation of meprobamate has been developed. After administering the drug to humans, about 12 percent of meprobamate is excreted unchanged and 40 percent as a conjugated compound.

Epinephrine and norepinephrine: A method for the estimation of metanephrine (3-O-methyl epinephrine) and normetanephrine (3-O-methyl norepinephrine) has been developed. After the administration of l-epinephrine to rats, 3 percent of the compound was excreted as metanephrine glucuronide. The administration of metanephrine resulted in the excretion of 5 percent metanephrine and 30 percent metanephrine glucuronide. When rats were pretreated with iproniazid, a monoamine
Part A. Project Description (continued)

oxidase inhibitor, the excretion of free and conjugated metanephrine was doubled. Similar results were obtained with norepinephrine. These observations suggest the following pathway for the metabolism of catechol amines in the rat:

\[
\text{Epinephrine} \xrightarrow{O\text{-methylations}} \text{metanephrine} \xrightarrow{\text{conjugation}} \text{metanephrine glucuronide} \\
\downarrow \\
3, \text{ methoxy-4-hydroxymandelic acid} \\
\uparrow \\
\text{Norepinephrine} \xrightarrow{O\text{-methylations}} \text{normetanephrine} \xrightarrow{\text{conjugation}} \text{normetanephrine glucuronide}
\]

Significance to Mental Health Research: These studies should provide basic information about the physiological disposition, metabolic fate, and mechanism of action of drugs affecting the nervous system.

Proposed course of project: The fate of ergot alkaloids (ergonovine, ergotamine), heroin, meprobamate, epinephrine, norepinephrine and other drugs acting on the nervous system will be studied.

Part B included Yes
Part B. Honors, Awards and Publications

Publications other than abstracts from this project:

Axelrod, J. and Inscoe, J.K. 1-(3'-methoxy 4'-hydroxybenzyl) 6-7 dimethoxy isoquinoline, a major metabolite of papaverine. Experientia, 8:319-320, 1957.


Honors and Awards relating to this project:

Part A.

Project Title: Cellular Mechanisms in the Metabolism of Drugs

Principal Investigator: Julius Axelrod

Other Investigators: Rudi Schmid and Gordon Tomkins

Cooperating Units: Metabolic Diseases Branch, NIAMD, Serial No.

Man Years (calendar year 1957): Patient Days
Total: 1 1/3 (calendar year 1957): None
Professional: 1/3
Other: 1

Project Description:

Objectives: This project is concerned with the enzymes involved in the transformation of drugs and hormones. We plan to study the metabolic pathways of drugs and hormones catalyzed by enzymes, and the intracellular localization, biochemical mechanisms, specificity and species distribution of these enzymes.

Methods employed: General biochemical and pharmacological procedures.

Major findings:

Glucuronide synthesis: We have found an enzyme that can synthesize a new type of glucuronide (N-glucuronides) as follows: Aniline + uridine diphosphate glucuronic acid (UDPGA) \(\rightarrow\) aniline N-glucuronide. Administration of aniline to guinea pigs resulted in the excretion of aniline N-glucuronide.

Methods for distinguishing ether, ester and N-glucuronides have been developed.

The enzymatic conversion of indirect reading (free) bilirubin to direct reading bilirubin (bilirubin glucuronide) has been demonstrated. This conversion is catalyzed by an enzyme in the liver microsomes and requires UDPGA.
Part A. Project Description (continued)

A biochemical lesion in non-obstructive, non-hemolytic jaundice in rat and man has been found. This disease arises from a marked deficiency in the glucuronide synthesizing enzyme. As a result, free bilirubin cannot be removed from the body by glucuronide conjugation.

O-Methylation of catechol amines: An enzyme that can O-methylate epinephrine and other catechols has been found. To carry out this reaction, the enzyme requires S-adenosylmethionine and a divalent metal. The enzyme is present in liver, lung, kidney, spleen, brain and intestines.

Significance to Mental Health Research: These studies may make some contributions to the understanding of metabolic mechanisms in health and disease.

Proposed course of the project: Enzyme systems involved in the metabolism of ergot alkaloids, diacetylmorphine and meprobamate will be studied. Further work will be done on the O-methylating enzyme.

Part B included Yes
Part B: Honors, Awards and Publications

Publications other than abstracts from this project:


Honors and Awards relating to this project:

Invited to give a paper on physiological significance of glucuronide conjugation at the Medicinal Chemistry Section, Gordon Conference, August, 1957.
Basic Research
Laboratory of Psychology
Section on Aging

BUDGET SHEET

Estimated Obligations for FY 1958

Total: $272,016
Direct: $173,424
Reimbursements: $98,592

Projects included: M-P-A 1 through M-P-A 12
Part A.

Project Title: Age Differences in the Behavior of the Rat; Learning and Transfer, and Psychomotor Behavior

Principal Investigator: Edward A. Jerome

Other Investigators: James E. Birren

Cooperation Units: None

Man Years:
  Total: 2.75
  Professional: 1.25
  Other: 1.50

Patient Days: None

Project Description:

Objectives: It is the purpose of this investigation to study those aspects of adaptability and psychomotor behavior that can be expected to manifest changes associated with chronological age and, from these studies, to construct a theoretical interpretation of the process of aging.

Methods Employed: A choice-escape apparatus utilizing light-aversion as drive has been employed in a series of ten experiments designed to study learning and transfer ability in two contrasted age groups of albino rats.

Major Findings:

1. Middle-aged and senescent rats were found not to differ significantly in respect to the relative frequency with which individuals reacted appropriately in the test situation under the light-aversion drive.

2. Functions describing the rate of acquisition of the basic operant have been inspected and no important qualitative or quantitative age differences have been found.
Part A. Project Description Continued

Major Findings Continued:

3. Observations have been made on the manner in which illumination regulates behavior in the test situation and no age differences have been found.

4. Two contrasting age groups have been tested with respect to their reaction to obstruction. Though these data have not yet been completely analyzed, inspection has failed to reveal any age difference in this connection.

5. Eighteen rats, divided among two age groups, have mastered a series of eight problems, very similar in form but providing ample opportunity for both positive and negative transfer. Though this constitutes less than half of the projected group, their data have been partially analyzed for the first two problems and reported in abstract. There were no age differences found in either learning or transfer.

Significance to the Program of Mental Health Research: The general indications of these experiments tend to confirm the currently growing conviction that if impairment in learning ability is common among aged humans it may well be due, not to a biological pre-destination created by the inevitable deterioration of living tissue in time, but to the effects of attitudinal or behavioral patterns adopted by maturing and aged individuals under the coercion of social conditions, customs and traditions. If such an interpretation is only partially true, to that extent the prospects for preventive and corrective procedures are more encouraging than they appear under the currently dominant explanation on the basis of decay of organization.

Proposed Course of the Project:

1. To continue the search for a problem complexity that shows an age difference in the learning ability of rats.

2. To activate a series of studies designed to indicate the influence of the time and type of passed experience on apparent age differences in the ability to learn.

3. To make additional studies of such behavioral factors as speed of response, fatigue, and psycho-motor adjustments to drug administration.

4. To initiate a series of studies designed to provide a basis of evaluating the appropriateness of the hunger drive in studies of aging (in animals).

Part B included—No.
Project Title: Age Changes in Time and Intensity Relations in Human Sensation, Perception, and Response

Principal Investigator: Alfred D. Weiss

Other Investigators: James S. Birren and Harry Kay

Cooperating Units: None

Man Years:
- Total: 1.75
- Professional: 1
- Other: .75

Patient Days:
- Inpatient Days: 63
- Outpatient Days: 63

Project Description:

Objective: The understanding of the psychological and physiological mechanisms in the change of stimulus perception and response time in human aging.

Methods employed: A. A click stimulator in which trains of clicks of varying length and speed were presented to determine certain limits of auditory perception. B. Simultaneous dichotic digit span presentations and conventional digit span presentations at various rates of speed to determine certain memory organization and interference effects. C. Delayed auditory feedback of speech to compare the effects of various delays on different age groups. D. The effects of chlorpromazine and secobarbital on delayed speech feedback. E. Reaction time with electromyographic measurements in ultra-short preparatory intervals.

Major Findings: Results thus far indicate that while there is no general decline in the limits of auditory temporal discrimination with age, perceptual loss increases with age with increasing loading of the perceptual mechanism. Perceptual change with rate of presentation is less than that due to age, rate changes affecting both age groups similarly. In this situation, where accuracy of response is highly stressed, response times of the two age groups do not differ significantly; while increasing the number of clicks as well as the rate of
Part A. Project Description Continued

Major Findings Continued: presentation significantly increase the response time for both groups.

In the drug study, chlorpromazine shows no effect on speech disruption, as here measured, while secobarbital shows dose related increased speech disruption. With practice, the amount of speech disruption is reduced under non-drug conditions.

Significance to the Program of Mental Health Research: These experiments indicate certain aspects of perceptual changes which occur with age in terms of handling various rates of information flow. They also give some indication as to the nature of sensory feedback control in speech.

Proposed Course of the Project: On those portions of the project on which data compilation is complete, statistical analyses will be undertaken. Certain other portions of this project have been initiated only recently and will be continued. It is proposed to further explore certain questions which have arisen as a result of these studies, both in human and in animal subjects.

Part B included—No
Part A

Project Title: Age Changes in Mental and Perceptual Abilities and Personality Structure.

Principal Investigator: Jack Botwinick

Other Investigators: James E. Birren

Cooperating Units: Home for the Jewish Aged, Philadelphia, Pennsylvania

Man Years: Patient Days:
Total: 3.5 Inpatient days: 600
Professional: 1.25 Outpatient days:
Other: 2.25

Project Description:

Objectives: The objective of this project is the description of normal age changes in mental functions and personality, and tentative interpretations of the antecedents and consequences of the changes. In addition, data were processed for correlations with physiological and psychiatric variables.

Methods Employed: Both standard and new procedures are used. These procedures include the WAIS, tests of problem solving, alternation, card sorting, perception of hidden figures; pencil and paper tasks such as slow and fast writing, connecting boxes by pencil line, mirror tracing; apparatus involving time measurements such as reaction time, with and without shock motivation, tachistoscopic presentation of perceptual material, and GSR conditioning. This latter procedure is done in cooperation with Dr. Conan Kornetsky, Laboratory of Clinical Science.

Major Findings: The major findings are that with normal aging there is: 1. a decrease in inhibitory processes and control functions that relate to motor, perceptual and cognitive abilities; 2. a relation between speed and accuracy of response as a function of stimulus
Part A. Project Description Continued

Major Findings Continued: difficulty, such that a factor or variable of "level of confidence required before making a discriminative response" is suggested, i.e., with age, it is possible that there is an increased tendency to take time to review the alternative choices before responding, that is relatively free from the necessity to do so from the point of view of accuracy of response; 3. an increased reaction time to shorter preparatory intervals in an irregular series. The latter suggests that either more time is required to get ready, or that more time is required to recover from the faulty expectancy.

Significance to the Program of Mental Health Research: These studies contribute to the description of normal aged and thus on what might be expected. Understanding the antecedent and consequent factors can aid in dealing with problems of the aged.

Proposed Course of Project: Studies will be enlarged for those variables that are found to be of significance in these preliminary studies of the aging process.

Part B included--Yes
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:


Honors and Awards relating to this project:

National Science Foundation Travel Award to Attend the IVth Congress of the International Association of Gerontology, July 14-19, 1957, Merano, Italy.
Project Title: Cytological and Cytochemical Changes in the Nervous System as a Function of Age: An Investigation of Submicroscopic Morphology Employing the Light and Electron Microscopes

Principal Investigator: William Bondareff

Other Investigators: None

Cooperation Units: None

Man Years:
- Total: 2.0
- Professional: .75
- Other: 1.25

Patient Days: None

Methods Employed: Employing Sprague-Dawley rats of varying age, various portions of the nervous system are surgically exposed and minute tissue samples are taken. Cerebral cortex, and spinal ganglion have in most cases been investigated. The specimens are fixed either with osmium tetroxide or by an improved method of freezing and drying, stained by a variety of electron microscopic "stains," embedded in plastic and sectioned by means of an ultramicrotome. Other specimens are prepared for study with the light microscope and serve as controls.

Major Findings: From light and electron microscope study of osmium fixed specimens of spinal ganglion from old rats it has been found that the intracellular pigment accumulating a function of age, so-called lipofuscin, does not originate due to mitochondrial degeneration as was previously thought. A mechanism of pigment derivation was
Part A. Project Description Continued

Major Findings Continued:

suggested whereby the pigment is thought to arise in association with the Golgi complex.

Some progress has been made in the application of freezing and drying to electron microscopic study of aged neurons and a few heavy metals, such as osmium, platinic tetrabromide, phosphotungstic acid and silver nitrate have been studied in relation to the study of the pigment and the submicroscopic morphology of the cytoplasm of aged neurons.

Significance to the Program of Mental Health Research: An understanding of the submicroscopic morphology of the neurons of the central nervous system as a function of age will be required for any definitive explanation of aging in the nervous system, for the functional activity of the brain is ultimately related to integration of its cellular units.

Proposed Course of the Project: After fixation and staining methods have been further developed certain cytochemical techniques of light microscopy will be applied to the electron microscope problem in attempt to further understand the chemical constitution of such age-associated intracytoplasmic inclusions as pigment and also to explore possible changes in other intracellular substances such as enzymes and glycogen as a function of aging. Morphological investigations, employing heavy metal staining of frozen-dried material will be directed toward an investigation of possible age changes in the submicroscopic morphology of the extracellular components of nervous tissue and their effect on intracellular processes. Also the change in intracellular water as a function of age will be investigated morphologically with the electron microscope.

The employment of a small, relatively simple nervous system in a study of submicroscopic morphology would be most desirable. An attempt will therefore be made to extend these studies so as to include invertebrate material. With such a morphological study of invertebrate nervous tissue, an adjuvant investigation of aging in invertebrate animals is also planned.

Part B included—Yes
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:


Honors and Awards relating to this project:

National Science Foundation Travel Award to Attend the IVth Congress of the International Association of Gerontology, July 14-19, 1957, Merano, Italy.
Part A.

Project Title: Age Changes in Brain Electrolytes in the Rat

Principal Investigator: Eugene Streicher

Other Investigator: None

Cooperating Units: None

Man Years: Patient Days: None
  Total: 1.08
  Professional: .33
  Other: .75

Project Description:

Objective: To measure age changes in the concentration of sodium, potassium, calcium, magnesium, chloride, aluminum, and silica in rat brain as a function of age.

Methods Employed: Sodium and potassium are measured by flame photometry, magnesium, calcium, phosphate, aluminum, silica, and chloride by suitable colorimetric methods.

Major Findings:

1. In all age groups, from 1 month to 2-1/2 years, the calcium content is very variable, the two halves of the same brain often differing from each other by several hundred percent. An elevated calcium level is not necessarily related to the age of the rat.

2. The calcium content of the two halves of the same brain are more closely related to each other in the brain of old rats than in young animals regardless of the level observed.
Part A. Project Description Continued

Major Findings Continued:

3. The calcium content of the brain parenchyma is approximately 2 milliequivalents/kilogram fresh weight. Additional calcium probably represents deposition in non-neuronal brain structures such as the blood vessels.

4. The magnesium content of the brain is somewhat diminished in rats over 2-1/2 years old.

5. Brain mitochondria, isolated from both young and old animals possess approximately the same concentrations of calcium and magnesium. The calcium content of isolated brain mitochondria is sufficiently high to account for almost all of the calcium of rat brain.

Significance to the Program of Mental Health Research:

1. These studies have demonstrated that the intracellular magnesium content is very high, possibly 30 milliequivalents/kilogram of neuronal protoplasm, and explains the need for the addition of relatively large amounts of magnesium to brain homogenates and mitochondria to secure maximal rates of respiration and oxidative phosphorylation. The magnesium content of brain structures can be utilized as a measure of cellular protoplasmic mass and can possibly be employed to evaluate the extent of demyelination in neurological disease.

2. The decreased magnesium content of brains obtained from animals over 2-1/2 years of age indicates that advanced age in rats may be accompanied by the loss of neurons and parallels morphological observations made on human autopsy material.

3. The observations on the variability of calcium in rat brain explain the divergent results on brain calcium levels reported in the literature over the course of the last fifty years and helps to elucidate the purported effects of vitamin D deficiency and low calcium diets on the calcium content of rat brain. Also, it sheds some light on the contradictory results published on the effects of parathyroidectomy on brain calcium level.

4. This work suggests that the rat may be employed in studies concerning the relationship of diet and genetic predisposition to calcium deposition in the brain.
Part A. Project Description Continued

Proposed Course of the Project: In addition to the measurement of age changes in other electrolytes of rat brain, analyses of calcium and magnesium will be carried out on several species of laboratory animals to provide control data for future studies on aging.

Part B Included--Yes
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:


Streicher, E. Biochemical investigations of the aging nervous system. In Press.

Honors and Awards relating to this project: None
Part A.

Project Title: metabolism of Nervous Tissue as a Function of Age

Principal Investigator: Joel Garbus

Other Investigators: None

Cooperating Units: Dr. E. Weinbach of the Laboratory of Tropical Disease continues to cooperate in certain aspects of this investigation

Man Years: Patient Days: None
Total: .63
Professional: .33
Other: .50

Project Description:

Objective: The objective is to measure alterations in the metabolic characteristics of nervous tissue as a function of age.

Methods Employed: Metabolic activity of rat nervous system preparations is measured in vitro under a variety of experimental conditions. The activities of enzymes are measured spectrophotometrically or manometrically. Tracer equipment has been installed for the study of relative metabolic rates using radioactive isotopes.

Major Findings: Observations on the respiration and oxidative phosphorylation of brain homogenates as a function of age have been extended to include measurements employing cellular particulates. A preparative procedure was developed for the isolation of cellular particulates of high metabolic activity and exceptional stability. Respiration and oxidative phosphorylation have been studied employing mitochondria prepared by these methods from the central nervous system of rats of various ages. No decline with age has been found in either respiration or phosphate esterification and no significant changes were found in the ability to utilize various substrates and in the stability of the mitochondria.
Part A. Position Description Continued

Major Findings continued:

These cellular metabolic activities are measured under optimum conditions, in vitro; an ample source of substrate, necessary co-factors, inorganic salts and buffers are supplied to the tissues. Permeability and diffusion barriers are minimized. Under these "ideal" conditions, the implication of our findings is that the enzymatic potential involved in these important metabolic processes are unimpaired with age. Of course, these model conditions, are not directly comparable to those pertaining in vivo.

Significance to the Program of Mental Health Research: The metabolism of neurons provides the energy required for cellular activities and directly supports functional nervous processes. A study of the metabolic potential of excised tissue may indicate whether the functional aspects of aging are related to quantitative or to specific deficiencies in the energy producing systems of the nerve cell.

Proposed Course of Project: It is proposed to continue these studies under restricted or less than ideal biochemical conditions; e.g., low oxygen tension, absence or diminution of substrate and co-factors electrical "stimulation" of brain slices; to reproduce, in vitro, a deleterious cellular environment as it were, which may be a factor in senescence. In addition, specific enzymes, which occupy important roles in cellular metabolism and neuronal activity, such as hexokinase, cholinesterase, monamine oxidase, will be measured.

Part B included—Yes
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project: None

Honors and Awards relating to this project:

National Science Foundation Travel Award to Attend the IVth Congress of the International Association of Gerontology, July 14-19, 1957, Merano, Italy.
Project Title: The Metabolism of Neuropharmacological Agents as a Function of Age

Principal Investigator: Joel Garbus

Other Investigators: None

Cooperating Units: None

Man Years: Professional: .33
Other: .25

Patient Days: None

Project Description:

Objective: The objective is to measure the rate of detoxification of neuropharmacological agents as a function of age and to relate the intensity and duration of the effects on the central nervous system with blood levels of the administered drug.

Methods Employed: An appropriate dose of a neuropharmacological agent is administered, and the blood levels measured at various times thereafter. Concomitantly, the effect on the central nervous system, i.e., duration of anesthesia or spontaneous activity is noted. Behavioral criteria are being surveyed and developed for the purpose of establishing measures of age changes in reactivity of the nervous system to neuropharmacological agents.

Major Findings: Previous work was concerned with the effects of age and sex on the duration of anesthesia induced in rats by two dissimilar agents: hexobarbital, a short acting barbiturate and hyroxydione (Viadril), a water soluble steroid. In the current investigation ethchlorvynol (Placidyl), a chlorinated acetylenic carbinol is being employed. The unique physical properties of the drug have necessitated the development of a new method for its preparation for injection. The accumulation of data is now in progress.
Part A. Project Description Continued

Significance to the Program of Mental Health Research: These studies should demonstrate whether alterations in the functional effects of drugs that occur with advancing age are due to an altered sensitivity of the brain, or to changes in the detoxification potential of the body. The fundamental research should provide a rational basis for future application of neuropharmacology to aged persons.

Proposed Course of Project: Studies on the effects of age and sex on the duration of anesthesia are being extended utilizing various hypnotic drugs that are chemically dissimilar, are detoxified through divergent mechanisms, and which may exert their effects on different parts of the central nervous system. In addition the effect of drugs in modifying behavior in physiological tests such as hearing will be measured.

Part B included—No
Part A.

Project Title: The Effects of Hypoglycemia, Anoxia, and Drugs on the Phosphocreatine Content of Rat Brain in Animals of Different Ages

Principal Investigator: Eugene Streicher

Other Investigator: None

Cooperating Units: None

Man Years:
- Total: .53
- Professional: .33
- Other: .25

Patient Days: None

Project Description:

Objective: To measure the relative rates of utilization and synthesis of phosphocreatine by rat brain in vivo as a function of age in various physiological states.

Methods Employed: Phosphocreatine will be measured as acid labile phosphate at room temperature in the presence of molybdate.

Major Findings: Methods are now being developed to measure phosphocreatine in the presence of inorganic phosphate and adenosine triphosphate.

Significance to the Program of Mental Health Research:
These experiments should elucidate the possible differential effects of age on the relative rate of energy utilization and production by rat brains in vivo.

Proposed Course of Project: After control values for phosphocreatine have been established for rats of different ages, the effects of drugs, anoxia, etc., will be ascertained.

Part B included--No.
Part A.

Project Title: The Effect of Age on the Distribution of Glucose Between Blood and Brain

Principal Investigator: Eugene Streicher

Other Investigators: None

Cooperating Units: None

Man Years: Total: .58 
Professional: .33 
Other: .25

Patient Days: None

Project Description:

Objectives: To determine the effects of age on the movement of glucose from the blood into the brain and the relationship between the free glucose level in the brain and the concentration of glucose-6-phosphate in that organ.

Methods Employed: "True" blood and brain glucose levels will be measured by means of glucose oxidase and the Nelson-Somogyl glucose method. Glucose-6-phosphate will be assayed with glucose-6-phosphate dehydrogenase.

Major Findings: A method for the extraction of glucose from brain tissue has been devised for the present investigation and optimal conditions for the measurement of glucose with glucose oxidase have been established.

Significance to the Program of Mental Health Research: Glucose is the main substrate of brain from which energy is derived for functional activity. However, the level of free glucose in the brain is exceptionally low, i.e., about 8 mgm.% in rats, suggesting that the metabolism of parts of the brain may be regulated by the ambient glucose supply. By employing animals of different ages subjected to various physiological conditions factors governing the transport of glucose into the brain from the blood may be studied. Also the
Part A. Project Description Continued

Significance to the Program of Mental Health Research Continued: relationship between brain glucose and glucose-6-phosphate should yield information on the kinetics of brain hexokinase activity in vivo and on the "permeability" of brain cells to glucose under different physiological conditions. It has been suggested that the mild form of diabetes often associated with aging is a homeostatic response to a decreased permeability of the brain to glucose.

Proposed Course of Project: After normal values for blood glucose, brain glucose and glucose-6-phosphate have been established, the effects of hypoglycemia and hyperglycemia will be ascertained.
Part A.

Project Title: Components of Cellular Structure as a Function of Age

Principal Investigator: Joel Garbus

Other Investigators: None

Cooperating Units: None

Man Years:
- Total: .58
- Professional: .33
- Other: .25

Patient Days: None

Project Description:

Objective: To determine if there are quantitative and qualitative variations with age in certain chemical components of cellular structure and in their biochemical activity in the nervous system.

Methods Employed: Spectrophotometric, colorimetric, chromatographic and electrophoretic methods for specific components will be employed. Tracer equipment, currently installed in the laboratory, utilizing radioactive isotopes may be used. Nervous tissue will be excised from rats of the colony of the Section on Aging.

Major Findings: Specific, sensitive colorimetric methods have been developed for the extraction and estimation of the nucleic acids in nervous tissues. Modifications have been made in the Kjeldahl nitrogen method to provide a rapid estimation of nitrogen in small amount of nervous tissue.

Using these methods, values are being established for the nucleic acid and nitrogen content of whole brain and cellular particulate preparation from normal, adult rats. These values will be used as a basis for comparison with tissues from senescent animals.
Part A. Project Description Continued

**Significance to the Program of Mental Health Research**: One of the difficult problems of biological research in gerontology is to determine whether the changes observed in the functioning of nervous tissue are due to alterations in the quantities or of various components to their changed biochemical activity. These investigations should provide some answers to this problem.

**Proposed Course of Project**: Determinations will be extended to senescent animals. In addition, methods for other components may be developed and employed.

Part B included--No
Part A.

Project Title: Preparation of a Handbook of the Behavioral Aspects of Aging

Principal Investigator: James E. Birren

Other Investigators: Jack Botwinick, William Bondareff, Edward Jerome, Harry Kay, and Alfred Weiss

Cooperating Units: None

Man Years: Patient Days: None
  Total: 2
  Professional: 1.50
  Other: .50

Project Description:

Objective: The purpose of this project is to organize existing scientific and professional knowledge about the behavioral aspects of aging. The material will be published in the form of a handbook which would represent an authoritative technical summary suitable for use by graduate students and professional persons.

Method Employed: The principal investigator will edit the volume and individual members of the Section will prepare selected chapters. There will be in addition approximately 18 chapters prepared by non-Federal employees. Organization of this project is done in collaboration with the University of Michigan (Project 3M-9118).

Major Findings: A suggested chapter outline was prepared by the editor and circulated to invited authors, who prepared more detailed outlines. These author outlines were exchanged among the authors to reduce overlapping material.

Significance to the Program of Mental Health Research: Problems of older persons are receiving increasing attention. The nature and scope of these problems involves basic biological and psychological changes as well as social circumstances. If rational methods of meeting mental health problems of older persons are to be advanced, it is necessary to take initial steps such as the present one which is to prepare a basic collection of facts.
Part A. Project Description Continued

Significance to the Program of Mental Health Research Continued: and interpretations of existing data. It is expected that the availability of this handbook will have an impact not only on training but also on current mental health concepts and practices.

Proposed Course of Project: Authors are now in the process of reviewing the literature and preparing their chapters. The current deadline for initial chapter drafts is February 1, 1958. Final manuscripts should be received by June 1958. The volume should be finished for submission to the printer by December 1958.

Part B included—No.
Part A,

Project Title: Electrophysiologic Correlates of Sensation and Perception

Principal Investigators: Alfred D. Weiss, and Robert Cohn

Other Investigators: None

Cooperating Units: National Naval Medical Center, Department of Electroencephalography

Man Years: Patient Days: None
     Total: .75
     Professional: .25
     Other: .50

Project Description:

Objective: To find electrophysiologic correlates of sensation and perception, using aging as the major variable when feasible.

Methods Employed: Microelectrodes were inserted into the retina and optic tract of a curarized cat, and white and color-filtered lights were flashed into the eye. Records were obtained at steady state (flashes about every 3 seconds over a prolonged period) and during dark adaptation.

Major Findings: Results are now being analyzed.

Significance to the Program of Mental Health Research: Information obtained through such experiments will help to elucidate the relationships between certain aspects of behavior and certain functions of the central nervous system.

Proposed Course of the Project: Operant conditioning techniques are now being devised to permit psychophysical and perceptual measurements on rats of various ages. Chronic microelectrode implantations for the recording of electrophysiologic correlates of psychologically determined differences will then be undertaken.

Part B included—No.
NATIONAL INSTITUTE OF MENTAL HEALTH

Basic Research
Laboratory of Psychology
Section on Animal Behavior

BUDGET SHEET

Estimated Obligations for FY 1958
Total: $184,652
Direct: $108,873
Reimbursements: $75,779

Projects included: M-P-B 1 through M-P-B 9
Part A.

Project Title: The analysis of the relationship between emotional behavior and certain cortical and subcortical structures in the subhuman primate brain.

Principal Investigator: H. Enger Rosvold

Other Investigators: None

Cooperating Units: None

Man Years: 2
  Professional: 1/2
  Other: 1 5/8

Patient Days: None

(1/3 NIMH Fellow in addition)

Project Description:

Project: To identify the emotional behavior which is subserved by various brain structures.

Objectives: To demonstrate in standard behavioral situations which elicit emotional approach and avoidance behavior the effects of electrically stimulating or ablating structures in brains of monkeys and chimpanzees.

Methods Employed: Animals are trained in special situations designed to elicit certain types of emotional behavior, following which various brain structures are electrically stimulated or destroyed. Sexual activity and conditioned fear, exemplifying emotional approach and avoidance behavior, respectively, will be the principal behaviors observed. The amygdala, hippocampus, and central gray will be the principal structures stimulated or ablated.

Major Findings: Funds and personnel have been insufficient to pursue this aspect of the program as actively as was anticipated. Consequently, construction of the equipment necessary for conditioned avoidance studies has not been completed. However, three pairs of animals have been tested preparatory to a sex-behavior study, the purpose of which is to explore the effect on such behavior of psychopharmacological drugs and brain lesions. It is anticipated that the physiological manipulations will start soon.

Significance to Mental Health Research: A careful description of the relationships between the brain and emotional behavior is fundamental to an understanding of mental health and disease.
Part A. Project Description Continued

Proposed Course of Project: Various brain structures will be systematically ablated or stimulated and various drugs will be administered in conjunction with systematic observations of emotional behavior.

Part B included Yes ___ No X
Part A.

Project Title: The analysis of the relationships between problem-solving behavior as demonstrated in the delayed response and discrimination tasks and certain cortical and subcortical structures in the subhuman primate brain.

Principal Investigator: H. Enger Rosvold

Other Investigators: None

Cooperating Units: None

Man Years:
- Total: 2
- Professional: 1/2
- Other: 1 1/2

(1/3 NIMH Fellow 1 Research Associate in addition)

Project Description:

Project: To identify the brain structures that are essential for delayed-response types of functions and to describe the changes in this behavior which follow lesions in these structures.

Objectives: To determine the cerebral organization subserving problem-solving behavior and to describe the nature of the behavioral dysfunction which follows damage to this organization.

Methods Employed: (1) Chimpanzees. Chimpanzees are trained on a variety of delayed-response tasks, operated in the prefrontal lobes, retested and sacrificed.

(2) Monkeys. Lesions are placed in those subcortical structures which have been shown to be important for delayed-response-type functions. The animal's performance is compared with that of monkeys and chimpanzees which have lesions in the prefrontal lobes. The animals are tested on a variety of tasks intended to specify the nature of the deficit which they incur. Automatic testing devices which will enable a much more thoroughgoing analysis of this behavior are being developed.

Major Findings: (1) Chimpanzees. In additional animals it has been confirmed that, as in monkeys, the performance of the chimpanzees on delayed-response-type problems is
Part A. Major Findings Continued

is impaired following damage to the prefrontal lobes. Unlike monkeys, however, they recover from the effects of the damage and after considerable retraining approach their preoperative level of performance. These findings provide a possible explanation for the apparent differences in the effects of frontal lesions in monkeys and man, viz; a more highly developed brain of man or chimp, the effect of damage to a particular area may be less than in the more primitive brain.

(2) Monkeys. It has been confirmed that lesions in the head of the caudate nucleus have effects on delayed-response-type functions similar to those of frontal lobe lesions. It has been found in addition that damage to other subcortical structures, specifically those related to the hippocampal formation, may have a similar effect. Automatic testing devices have now been developed which will make it possible to compare directly animals with lesions in one or the other of these apparently related structures and to study in considerably more detail the role that each of these structures plays in problem-solving behavior.

Significance to Mental Health Research: A careful description of the relationships between the brain and problem-solving behavior is fundamental to an understanding of those processes which limit or reduce intellectual capacity, i.e. mental deficiency, brain injury, brain disease, etc. That part of the study dealing with chimpanzees suggests that rather severe damage can be inflicted on the frontal lobes without permanently impairing problem-solving behavior. That part of the study involving monkeys points up the importance of deep-lying subcortical structures in intellectual types of behavior. This latter point has generally been neglected in considering the causes of impaired intelligence.

Proposed Course of the Project: (1) To explore in additional chimpanzees the effects of frontal lesions on other types of tests. (2) To specify more exactly the subcortical structures involved in problem-solving tasks, and where possible to specify the relationships between these structures. (3) To compare the effects of lesions in these structures on problem-solving and other types of tasks designed to make explicit the nature of the deficit following such lesions. This will involve primarily the acquiring of automatic testing devices and adapting them for use in these problems.

Part B included Yes X No
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:


Honors and Awards relating to this project:
Part A.

Project Title: The effects of brain lesions and immediate post-operative experience on dominance behavior in primates.

Principal Investigator: Allan F. Mirsky

Other Investigators: None

Cooperating Units: None

Man Years: Total: 5/6
Professional: 1/3
Other: 1/2

Patient Days: Total: None

Project Description:

Project: The effects of brain lesions and immediate postoperative experience on dominance behavior in primates.

Objectives: There are two main objectives in this project: (A) To compare the effects of frontal and temporal lesions on social behavior in monkeys and chimpanzees. (B) To modify in predicted directions the dominance behavior of monkeys with temporal lobe lesions.

Methods Employed: Groups of monkeys and chimpanzees are studied carefully before and after selected members of such groups are subjected to surgical or stereotaxic electrolytic lesions. In some studies the monkeys are given immediate postoperative experience designed to make them either fall or rise in dominance.

Major Findings: To date, two chimpanzee colonies have been studied. One member of each of these three-animal colonies has been subjected to either a bilateral prefrontal lobotomy, a bilateral anterior temporal lesion or a bilateral ventral temporal lesion. The temporal lesions appear to have had little, if any, consistent effect on dominance. The frontal lesions, on the other hand, produced a marked, although temporary, decrease in dominance in both animals. The findings in the chimpanzee groups stand in sharp contrast to the results of similar investigations conducted in monkeys: dominance in chimpanzee groups, as measured by food-getting, is considerably more variable than that found in monkey
Part A. Major Findings Continued

groups; the anterior temporal-lobe lesions that usually produce marked changes in dominance behavior in monkeys are apparently without effect in chimpanzees; the frontal lesions which usually produce increased dominance in monkeys appear to have an effect in the opposite direction in chimpanzees.

With respect to dominance behavior in monkeys with temporal lobe lesions, the following are the major findings to date: Nine colonies have been studied, and the behavior of those animals whose postoperative behavior has been manipulated conforms fairly well to predictions, i.e., animals with amygdala lesions that are placed in a postoperative environment designed to maximize their dominance do not fall in dominance and may even rise in dominance when returned to their original groups. In a corollary investigation it was found that bilateral stereotaxic ablations in the hippocampus are without effect on dominance behavior in monkeys. This suggests that the behavioral consequences of amygdala and hippocampal ablations may be quite different, despite the fact that anatomi- cally and physiologically these two structures are closely re- lated.

Significance to Mental Health Research: This project should provide more information about the relationship between brain function and social behavior in several primate species. Experimental evidence has already been provided that the effects of a brain lesion on social behavior cannot be evaluated independently of the total social situation of which the subject is a part.

Proposed Course of Project: Another three-animal chimpanzee group is under study at the present time. Eventually, two of these animals will receive bilateral frontal lesions; if the finding of the first chimpanzee study is reliable, both animals should exhibit some postoperative depression in dominance. Unfortunately, the monkey dominance studies must be curtailed until additional funds and personnel are made available to the Section.
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:


Part A.

Project Title: Further analysis of the Continuous-Performance technique as a research tool and diagnostic device in assessing the effects of drugs and brain pathology.

Principal Investigator: Allan F. Mirsky

Other Investigators: None

Cooperating Units: Walter Reed (ARMC), Neurological Surgery NINDB, Clinical Science NIMH

Man Years:
Total: 1 1/3
Professional: 1/3
Other: 1

Patient Days:
Total: 400

Project Description:

Project: Further analysis of the Continuous-Performance technique (C.P.T.) as a research tool and diagnostic device in assessing the effects of drugs and brain pathology.

Objectives: The objectives of this project include three related areas of investigation: (1) To assess the effects of various types of brain pathology on functions measured by the C.P.T. (2) To investigate the effects of drugs on the C.P.T., so as to gain information relative to the functions and brain locus or loci tapped by the C.P.T. (3) To explore the usefulness of the C.P.T. as a diagnostic device.

Methods Employed: Individuals with brain pathology and normal and pathological controls are tested under various conditions, including drugs, on the C.P.T. and other standard measures of intellectual functioning.

Major Findings: In the research conducted to date, several groups of individuals have been studied. These include approximately 150 patients from the Surgical Neurology Branch, NINDB (involving 400 patient hours) and approximately 100 normal volunteer controls (involving 550 subject hours). The major findings may be summarized as follows:
Part A. Major Findings Continued

A. The C.P.T. apparently can distinguish reliably between patients with presumed subcortical pathology and those with focal cortical pathology. The 'subcortical' group appears to be impaired on this test, even after statistical control of related variables such as I.Q., age, frequency of seizures, duration of illness, and degree of E.E.G. abnormality. These findings were gathered on 76 patients selected on the basis of more or less clear-cut cortical or subcortical pathology.

Approximately 30 patients have been tested with the C.P.T. before and after unilateral cortical resections. These removals seem to have no effect on C.P.T. performance.

C. The effects of a number of centrally-acting drugs on the C.P.T. have been measured, using normal controls and a small group of schizophrenics. These studies have been conducted on patients made available by the Laboratory of Clinical Science. Meprobamate (Miltown) as well as chlorpromazine produces impairment on the C.P.T., although the magnitude of the effect produced by meprobamate is much less than that produced by chlorpromazine. Other centrally-acting drugs, including L.S.D., meperidine, secobarbital, phenobarbital, and d-amphetamine are without effect on the C.P.T. In a group of 14 schizophrenic patients studied at NIE, there was a great range in performance and a curious finding of no significant impairment produced by chlorpromazine.

D. A group of 36 normal-aged patients were tested on the C.P.T. As was the case with other psychological tests given to this population, there was a marked spread in performance, from those who perform as well as young normal patients to those who appear as impaired as some of the brain-damaged population. Comparison of C.P.T. scores with the tests given these individuals by other investigators reveals significant correlation with tests of reaction time, line difference limen and the Wechsler Adult Intelligence Scale subtests of arithmetic and digit-symbol substitution. These significant correlations are compatible with the conception that the test is a measure of 'attention'. The fact that none of these correlations accounts for more than 25% of the observed variance, however, suggests that the C.P.T. is measuring something not tapped by the other tests.

Significance to Mental Health Research: The information gathered to date on the effects of centrally-acting drugs, brain-damaged patients, and sleep-deprivation (in studies done at Walter Reed Army Medical Center) suggests that the C.P.T., as might be expected in the case of all tests involving attention, is particularly sensitive to alteration in the functioning of mid-brain subcortical structures.
Part A. Significance to Mental Health Research Continued

Application of this technique to various pathological groups may help to elucidate the role and/or importance of subcortical interference in such disease entities as epilepsy and, possibly, various psychopathological conditions in which the influence of brain damage is not well understood.

Proposed Course of Project: Epileptic and other neurological patients will be tested with the C.P.T. and other procedures before and after brain surgery, in an attempt to replicate the findings previously obtained with this population. A study is currently in progress on the effects of other centrally-acting drugs including alcohol, benzactyzine and d-amphetamine. A particular question being investigated concerns whether the stimulant, d-amphetamine, can reverse the deleterious effects on the C.P.T. produced by 72 hours of sleep deprivation. When the facilities and positions at St. Elizabeth's Hospital become available, effort will be made to investigate systematically in psychotic patients the effects of the centrally-acting drugs previously studied in normal individuals. The performance of schizophrenics under chlorpromazine will be of particular interest, in view of the preliminary finding obtained at NIH.

Part B included Yes X No
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:


Honors and Awards relating to this project:
Part A.

Project Title: Defining an extrageniculostriate system in vision

Principal Investigator: Mortimer Mishkin

Other Investigator: None

Cooperating Units: None

Man Years: Professional: Other:
Total: 1 1/3 1/3 1
Patient Days: Total: None

(1/3 NIMH Fellow in addition)

Project Description:

Project: The neural components of an extrageniculostriate system in vision.

Objectives: Evidence of severe visual impairment following damage to inferotemporal neocortex in monkeys suggests that the inferotemporal region and the primary visual system are closely related. How they might be related is not known. The possibility that either the prestriate cortex, the pulvinar, or the superior colliculus serves as the essential relay station between the primary visual system and inferotemporal cortex has been tentatively eliminated by previous work. Other possibilities, currently being tested, are that (1) the three foregoing structures serve as alternate relay stations such that any one may serve the relay functions of the others or (2) temporal cortex and primary visual cortex are linked directly by long association tracts.

Methods Employed: Monkeys are subjected to combined destruction of (1) prestriate cortex, pulvinar and colliculus or (2) unilateral temporal cortex, contralateral occipital cortex, and corpus callosum. The attempt in both experiments is to isolate intact temporal cortex from intact occipital cortex. The operated animals are then tested on visual tasks known to measure reliably the effects of bilateral inferotemporal or bilateral lateral occipital (macular projection) lesions.

Major Findings: (1) Combined electrolytic destruction of the pulvinar and colliculus has been accomplished by directing the electrode into these nuclei at an oblique angle.
Part A. Major Findings Continued

(Use of the simpler vertical approach resulted in severe subcortical vascular lesions from which several animals never fully recovered.) Thus far the effects of combined pulvinar and collicular lesions on visually-guided behavior appear to be negligible. The next step, i.e., destruction of these nuclei in combination with removal of the prestriate cortex, will soon be attempted.

(2) Animals with the second combination of lesions are now being tested and appear to be markedly impaired.

Significance to Mental Health Research: Vision is perhaps the best understood of the sensory modalities in relation to the functioning of the nervous system. Yet a major problem remains unsolved in vision as it does in all sensory modalities: Delineation of the events which intervene between stimulus reception at the cortex and the observed response. The demonstration that damage to the inferior convexity of the temporal lobes in monkeys produces impairment in visually-guided behavior has opened up the hitherto inaccessible area of the intracerebral processes in vision, i.e., neural activity related to vision but beyond the level of the striate cortex. Unravelling these mechanisms in vision should aid greatly in the solution of a general problem for psychology, viz., accounting for the intervening neural processes (thought and its breakdown) in normal and abnormal behavior.

Proposed Course of Project: The two experiments outlined above will be continued to completion. For the first experiment this involves adding prestriate lesions to the subcortical damage; for the second, it involves replicating the original group of experimental animals and their various operated controls.

Part B included  Yes X No ___
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:


Honors and Awards relating to this project:
Part A.

Project Title: A comparative study in primates on the effects of temporal lobe damage on visually guided behavior.

Principal Investigator: Mortimer Mishkin

Other Investigators: None

Cooperating Units: None

Man Years: Patient Days:
Total: 5/6 Total: 200
Professional: 1/3
Other: 1/2

Project Description:

Project: Effects of temporal lobe damage on visually guided behavior in monkeys, chimpanzees, and man.

Objectives: Damage to the neocortex of the temporal lobes produces impairment in visually-guided behavior both in monkeys and baboons. This project attempts to determine whether similar impairment may be produced by temporal-lobe damage in the chimpanzee and in man.

Methods Employed: (1) Chimpanzees are trained on a variety of visual tasks (similar to those used with monkeys and baboons) before operation, after unilateral temporal neocortical damage, and after bilateral damage. Unoperated chimpanzees as well as chimpanzees with different cerebral lesions serve as controls.

   (2) Human subjects with focal temporal-lobe epilepsy are tested on a difficult visual discrimination task (analogous to the simpler tasks used with animals) before operation and/or after unilateral temporal-lobe surgery for relief of epilepsy. Patients with non-temporal-lobe epilepsy and non-temporal-lobe surgery serve as controls.

Major Findings: (1) Chimpanzees that were unaffected by unilateral damage have shown visual impairment following bilateral damage. Since control animals with bilateral damage to allocortical structures of the temporal lobes
Part A. Major Findings Continued

have remained relatively unimpaired, it appears that the visual impairment is selectively related, as it is in monkeys, to lesions in the neocortical region.

(2) On the basis of data gathered so far, patients with temporal-lobe epilepsy, with or without unilateral temporal-lobe surgery, have shown no deficit as compared with controls on the visual task.

Significance to Mental Health Research: The assumption underlying neuropsychological experiments conducted on animals, particularly rhesus monkeys, is that any brain-behavior relationship there discovered will contribute to an understanding of normal and pathological brain function in man. This assumption has been amply supported by comparative data on the functions of sensory and motor cortex. Now, reliable data are becoming available concerning the functions served in monkeys by "association cortex". This project attempts to apply these recent findings to aid the study of "association-cortex" functions in man. The chimpanzee, which may be considered to lie intermediate to man and monkey, both from an anatomical and a behavioral standpoint, serves as an experimental bridge in this comparative study.

Proposed Course of Project: (1) Additional operated and un-operated control animals will be added to the chimpanzee study and additional behavioral data will be gathered on the experimental animals in an attempt to define more precisely the extent and the nature of their visual impairment.

(2) The results of the chimpanzee study suggests that the difficulty in demonstrating visual disturbance in patients with temporal-lobe damage is due to the fact that such damage is rarely if ever bilateral and symmetrical. Recent work with monkeys, however, suggests that visual impairment after unilateral temporal lesions might be detected if vision is confined to the field opposite the injury. On this hypothesis an experiment has been set up to compare tachistoscopic recognition in the left and right visual fields in patients with left or right-temporal-lobe removals.

Part B included Yes ___ No X
Part A.

Project Title: Histological Analysis of Brain Lesions in Primates

Principal Investigator: Maria K. Szwarcbart

Other Investigators: None

Cooperating Units: None

Man Years: Professional: 1 Other: 1/2

Patient Days: Total: None

Project Description:

Project: (1) Analysis of the lesions which had been placed in monkeys and chimpanzees.

(2) Tracing caudate-frontal connections.

Objectives: The objective of the first part of this project has been to define the locus and extent of the different lesions that have produced similar deficits in the behavioral studies and of the second, to determine whether any anatomical relationship exists between the head of the caudate nucleus and cortex of the frontal lobes.

Methods Employed: Sixty-nine brains have been fixed in celluloidin or paraffin, sectioned, prepared with several stains, and examined microscopically. The results of these examinations have been translated into graphic representation by means of camera lucida drawings. In the second project, the brains of several monkeys with selective frontal lesions have been especially prepared to determine whether such lesions produce anterograde degeneration of fibers leading to the caudate nucleus and/or loss of cells in this nucleus.

Major Findings: In the first project it has been verified that lesions restricted to the head of the caudate nucleus result in deficits similar to those following damage to frontal cortex. (It is this finding which gave rise to the second
project.) The anatomical analysis has suggested further, that damage to other subcortical structures, e.g., the Ammonic Tract of Cajal, may also produce 'frontal-lobe signs'. On the other hand, these structures and others such as the superior colliculus and medial pulvinar have been eliminated in the search for areas related to temporal-cortex functions. The second project is not far enough along to have any definitive findings.

Significance to Mental Health Research: Information on the interrelationships among various brain structures is essential if normal and abnormal behavior are to be understood in terms of brain mechanisms and their breakdown. A systematic search for the different structures which serve similar behavioral functions, and the search for connections between these structures should help provide some of the needed information.

Proposed Course of Project: (1) The analysis of lesions which provide temporal and frontal-lobe symptoms will continue. Lesions designed to produce emotional changes similar to those produced by amygdalectomy will be added to the study.

(2) In addition to the study of anatomical connections between frontal cortex and the caudate nucleus (and other structures which appear to be related to frontal cortical functions), an exploration for possible direct connections between the temporal lobe and the visual system will soon be initiated.
Part A.

Project Title: Electroencephalographic correlates of sustained attentive behavior in man.

Principal Investigator: Allan F. Mirsky

Other Investigators: None

Cooperating Units: Neurological Surgery NINDB

Man Years: Patient Days:
Total: 5/6 Total: 15
Professional: 1/3
Other: 1/2

Project Description:

Objectives: This study is concerned with the relation between the E.E.G. and behavior on tasks requiring sustained attentiveness or vigilance during periods of time of varying length. Both brain-damaged and normal individuals will be studied; in the brain-damaged population, behavior concomitant with hypersynchronous discharges in the E.E.G will be of particular interest; with the normal subjects, the interest will be rather in behavior attended by alpha suppression or E.E.G. 'activation'.

Methods: Electroencephalograms and behavior of a continuous nature will be recorded simultaneously. Great flexibility in the nature of the task is afforded by means of a new projection instrument which permits stimulus duration to be varied almost continuously between intervals of 10 milliseconds and 10 seconds and interstimulus duration to be varied from 100 milliseconds to 10 seconds. In addition, the new device makes possible the presentation of continuously presented auditory stimuli, and possesses a number of features which facilitate the study of learning and motivational factors in this performance.

Major Findings: The instrument was delivered in September, 1957. The work with it to date indicates that it meets specifications and should prove useful in investigating the problems for which it was designed.
Part A. Project Description Continued

**Significance to Mental Health Research:** This research should provide information about the relationship between brain function, as measured with the E.E.G., and vigilant or attentive behavior. All information relating brain functioning to behavior contributes significantly to our understanding of those diseases which affect the behavior of man.

**Proposed Course of Project:** Normal and brain-damaged individuals will be studied with this technique and the records that are obtained will be carefully analyzed to ascertain the relationship between electroencephalographic phenomena and sustained attention. Some subjects with implanted electrodes being studied by the Surgical Neurology Branch for other purposes will also be used.
Part A.

Project Title: Electrical activity in temporal cortex during visual-discrimination learning and performance

Principal Investigator: Mortimer Mishkin

Other Investigators: None

Cooperating Units: None

Man Years: Patient Days:
Total: 1/3 Total: None
Professional: 1/3
Other: 0

Project Description:

Project: Correlation of electrical activity in temporal cortex with learning and performance on visual discriminations.

Objectives: Damage to inferotemporal neocortex in monkeys impairs their visual-discrimination learning and retention.

The purpose of this project is to determine whether or not similar impairment can be produced by electrical stimulation of the temporal cortex and also whether or not visual-discrimination learning is accompanied by changes in the electrical activity of this region.

Methods Employed: Surface electrodes are permanently implanted in the inferotemporal region. Animals are then trained to discriminate visual stimuli that are exposed briefly by a tachistoscopic projector. Automatic programming permits synchronization of the stimulus exposures with electrical stimulation or recording through the implanted electrodes.

Major Findings: No experimental data have been obtained. However, techniques have been developed for implanting electrodes and recording electrical activity during performance on a visual task. In addition, a tachistoscopic, single-framing, strip-film projector has been designed which meets all the necessary specifications. Apparatus for automatically programming the projector, training the animal and recording the animal's behavior has also been designed.
Part A. Project Description Continued

Significance to Mental Health: Ablation studies in monkeys have provided evidence that activity in inferotemporal neocortex may be one link in the chain of intracerebral processes serving vision. A study of the electrical activity in temporal cortex during performance on visual tasks should help to delineate the neural events underlying vision.

Proposed Course of Project: The experiments which have been outlined must await receipt and assembly of the equipment which has been designed.

Part B included Yes     No X
Basic Research
Laboratory of Psychology
Section on Perception and Learning

BUDGET SHEET

Estimated Obligations for FY 1958

Total: $104,936
Direct: $69,895
Reimbursements: $35,041

Projects included: M-P-L 1 through M-P-L 6
Serial No. M-P-L-1
1. Laboratory of Psychology
2. Section on Perception and Learning
3. Bethesda

PHS-NIH
Individual Project Report
Calendar Year 1957

Part A.

Project Title: Effects of Lysergic Acid Diethylamide (LSD-25) on Visual Functions.

Principal Investigator: V. R. Carlson

Other Investigators: Eugene Tassone

Cooperating Units: None

Man Years
Total: 83 1/3 %
Professional: 33 1/3 %
Other: Research Assistant: 33 1/3 %
Secretarial: 16 2/3 %

Patient Days
200 In-patients

Project Description:

Objective: LSD-25 produces various temporary distortions in vision when administered to normal human subjects. These distortions are said to be similar in many respects to distortions in perceptual processes often found in psychotic conditions, but the effects have been described for the most part in general subjective terms. The purpose of this project is to specify the effects of LSD-25 on visual and perceptual functions more precisely and quantitatively. During this past year the effort has been to determine the effects of LSD-25 on pupillary response and to compare them with effects of chlorpromazine, secobarbital, and meperidine.

Methods Employed: LSD is administered to normal volunteer subjects as one condition in a relatively long-term schedule of other drugs and placebo without the subject's knowledge of which condition is being administered on each particular occasion. The subject performs the same visual-perceptual tasks under control, placebo, and drug conditions, and the results are compared among these three situations.
Major Findings: Studies of the effects of LSD on the absolute visual threshold have been completed. The threshold was raised throughout the course of dark adaptation by a small but reliable amount, and the variability in the threshold values was not increased. In addition, the photopic threshold was affected significantly more than the scotopic threshold, strongly suggesting a cortical effect of the drug. Hallucinogenic effects were not observed in these subjects. Psychotic and neurotic patients have shown evidence of an elevated visual threshold, however, so that this effect of LSD may constitute another point of similarity between the effects of the drug in normal humans and the manifestations of more naturally occurring psychological disorder.

Significance to the Program of Mental Health Research: These studies provide basic data needed to evaluate comparisons between the effects of LSD-25 and other psychologically relevant drugs and between the effects of these drugs and certain psychological manifestations of psychotic conditions. In addition to interest in the psychopharmacological aspects of LSD itself, however, these studies are oriented toward the more general problem of differentiating aspects of perception which may be related to changes in the general psychological state of the individual from those which may depend more directly upon some particular neural function or structure and are relatively impervious to diffuse changes in psychological state. In this context LSD is viewed as one means of producing experimentally a change in the general psychological condition of the subject without causing any specific, circumscribed neural impairment.

Proposed Course of Project: Data will be obtained on more complex perceptual functions involving the integration of contextual cues, such as occurs in size-constancy and various visual illusions.

Part B. included: Yes [x] No [ ]
Part B. Honors, Awards, and Publications


Honors and Awards relating to this project: None
Project Title: Test of the Satiation Theory of Perception

Principal Investigator: V. R. Carlson

Other Investigators: Eugene Tassone

Cooperating Units: None

Man Years
Total: 75%
Professional: 33 1/3%
Other: Research Assistant: 33 1/3%
Secretarial: 16 2/3%

Patient Days
50 Out-patients

Project Description:

Objective: The object of this study is to devise a crucial test of Kohler's Theory of satiation by means of a figural-aftereffect experiment.

Methods Employed: The subject is first satiated by viewing a "satiation" stimulus pattern steadily for about one minute. Then he looks at a test stimulus; and any distortion in the perception of the test stimulus which is induced by the previous satiation is measured as the "figural-aftereffect".

In this study the experimental satiating stimulus is a moving field of curved lines, viewed by the subject with stationary binocular fixation. The control stimulus is a stationary field of
Methods Employed Continued: curved lines. In both cases the test stimulus is a single, stationary line of adjustable curvature. Under these conditions Köhler's theory would predict a figural-aftereffect in the control condition but not in the experimental condition, whereas a theory such as that of Hebb could account for figural-aftereffects in both conditions.

Major Findings: Data has been obtained on a number of subjects but the results have not yet been analyzed. The experiment is a very difficult one in terms of procedure and in terms of the performance required of the subject. Experience so far, however, indicates successful execution of the experiment.

Significance to the Program of Mental Health Research: Two important psychological theories of normal perception have been promulgated in recent years, that of Köhler and of Hebb. In many respects these two theories are alternative rather than complementary, and this experiment provides an important source of evidence for deciding between the two. In order to understand fully the distortion in perception which is found in mentally deranged patients, it is necessary to have a sound theory of the normal processes of perception.

But aside from these general theoretical considerations, the so-called phenomena of "cortical satiation" may prove to be more specifically important in studying the central neural processes underlying attention and short-term memory.

Proposed Course of Project: The experiment will be performed with a sufficient number of subjects for the results to be statistically reliable. Then, depending upon the findings, certain additional, related experiments may be necessary in order to develop a clear interpretation in terms of perceptual theory.

The findings will be utilized in designing future experiments oriented toward studying basic processes of attention and short-term memory in terms of possible underlying neural mechanisms.

Part B included: No
Part A.

Project Title: Electrical Recording of Eyemovements

Principal Investigator: V. R. Carlson

Other Investigators: None

Cooperating Units: None

Man Years
Total: 33 1/3%
Professional: 16 2/3%
Other: Secretarial: 16 2/3%

Patient Days
None

Project Description:

Objectives: The aim of this study is to develop a technically adequate means of recording eyemovements and eye position electrically.

Methods Employed: A corneo-retinal potential of approximately 25 to 500 microvolts is set up by an eyemovement, the exact value depending principally upon the magnitude of the eyemovement. This potential is picked up by electrodes placed on both sides of the eye, amplified, and led to a recording unit. The recorded values are calibrated with reference to some zero point in the visual field, and from the calibration one can determine where the eye was directed at a given time.

Major Findings: Certain difficulties with the apparatus have not been resolved, and thus far it has not been possible to obtain technically adequate measurements.
Part A. Project Description Sheet Continued

Significance to the Program of Mental Health Research: Eyemovement recording is potentially a valuable tool in measuring perceptual variables such as absolute and difference thresholds, discriminations, and complex patternings of perceptual response. Research in perception as it relates to personality maladjustment and mental disorder is concerned with the interaction between the individual's more or less unconscious motivations and his perceptions. Hence in many experimental situations it is desirable to be able to utilize a perceptual response which is not primarily determined by the subject's immediate conscious processes. Eyemovement recording may provide a feasible means of obtaining an indication of what the subject perceives and where and how he directs his attention in an appropriate experimental situation, relatively uninfluenced by his immediate conscious motivations.

Proposed Course of Project: The problem breaks down logically and practically into three stages:

1. Work out the technical apparatus problems. Progress is currently in this stage. The necessary items of equipment have been obtained and integrated into a functional system. The apparatus is at the present time undergoing a major technical check, repair, and modification in the Instrument Section.

2. Work out the methodology for measuring psychological variables by means of eyemovement recording.

3. Apply the methodology to specific problems in perceptual-attentional-motivational processes.

Part B included: No
Part A.

Project Title: Visual Discriminative Processes in the Pigeon.

Principal Investigator: Donald S. Blough

Other Investigators: William Jones

Cooperating Units: None

Man Years

<table>
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<tr>
<th>Total</th>
<th>216 2/3%</th>
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<tbody>
<tr>
<td>Professional</td>
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<td>Other: Research Assistant</td>
<td>100%</td>
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<tr>
<td>Secretarial</td>
<td>16 2/3%</td>
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Patient Days

| None |

Project Description:

Objectives: To continue to develop methods for the study of stimulus discrimination and generalization in pigeons; using these methods to describe the basic processes involved in stimulus control of behavior.

Methods Employed: Automatic apparatus and procedures developed in previous years are still in use. Newly developed behavioral techniques include a method for maintaining a continuous "standing" response, and a method for the intensive study of stimulus generalization in single animals.

Major Findings: Preliminary results, indicating that a dosage of LSD that has no gross behavioral effect on the pigeon raises its visual threshold substantially, were confirmed. Curves showing the...
Major Findings continued: extent and course of this threshold elevation were published. LSD was again shown to improve performance in a complex visual discrimination task.

The effects of several drugs on a delayed discrimination were determined. There was some indication that chlorpromazine produced a particular decrement in the birds' ability to "remember" a discrimination during a delay.

In contrast to the other procedures, which show decrements following administration of chlorpromazine, the ability of pigeons to "stand still" for food reward was markedly increased by this drug. Pentobarbital, which acts like chlorpromazine in several other situations, here produced opposite effects, reducing the ability to "stand still".

Generalization gradients relating response rate to visual stimulus intensity were determined. The gradients did not indicate an effect of stimulus intensity per se, contrary to prevalent theoretical notions. Pentobarbital and chlorpromazine had little or no effect on the gradients, suggesting that the effects of these drugs on discrimination is not a result of broadened generalization. Other gradients were determined which relate response rate to visual stimulus wavelength. An analysis of these results is in progress.

Significance to the Program of Mental Health Research: The overall aid of the project is to determine in what manner stimuli come to control "instrumental" or "operant" behavior - the sort of behavior that constitutes most of normal human activity. Maladaptive behavior may result from (among other things) the loss of certain stimulus controls, or from the presence of undesirable control. An understanding of this topic thus has fundamental importance to the understanding of behavior and its disorders. The project has contributed to the effort, now underway in many laboratories, to specify the behavioral effects of various drugs, especially the so-called "tranquilizers". The procedure outlined above in which the pigeon is trained to "stand still" may also prove valuable in selecting potential tranquilizers from among unfamiliar compounds.
Part A. Project Description Sheet Continued

Proposed Course of Project: During the next year, the broad exploratory study of drug effects will be curtailed. Drugs will be used on studies in which the earlier exploration has indicated that they may have some analytic value. Considerable effort will be devoted to the problem of relating discrimination and generalization.

Part B included: Yes
Part B. Honors, Awards, and Publications


Honors and Awards relating to the project: None
Part A.

Project Title: Individual Differences in Normal Perceptual Processes.

Principal Investigator: V. R. Carlson

Other Investigators: Eugene Tassone

Cooperating Units: None

Man Years

Total: 75%

Professional: 25%

Other: Research Assistant: 33 1/3%

Secretarial: 16 2/3%

Patient Days

50 Out-patients

Project Description:

Objectives: (1) To obtain normal control data for standardizing procedures and apparatus in the measurement of perceptual variables, (2) To investigate inter-relationships and consistencies of individual differences among basic perceptual processes and personality, emotional, and motivational variables.

Methods Employed: In the various perceptual situations the subject is required to view a given stimulus or pattern for a specified amount of time. The stimulus may vary in brightness, orientation, location, configuration, size, shape, or color. He then makes a perceptual judgment.
Methods Employed Continued: in one or more of these dimensions with respect to that or a subsequently presented stimulus. Personality data is obtained on each subject by means of standardized psychological tests. Studies in progress at the present time are concerned primarily with perceptual size-constancy and with several optical illusions. In the size-constancy task the subject is required to match in size a near, variable stimulus with a far, standard stimulus under two different instructional sets. One instruction (I) requires a match on the basis of perceptual appearance without regard to actual size; the other instruction (II) calls for a match according to actual size without regard to perceptual appearance. The optical illusions require judgments of length or shape in situations where these perceptual dimensions are distorted by the stimulus configurations employed.

Major Findings: Arrangements for obtaining normal subjects have only recently been completed, and only the most preliminary results have been obtained. It is quite clear, however, that Instructions I and II do tend to produce different behavioral responses in the size-constancy situation and that Instruction II manifests a strong component of performance or non-perceptual judgmental activity. This is not a necessary result by any means, and subjects who show less difference in the effects of the two instructional sets seem observationally to be different personality-wise from those who show a marked difference.

Significance to the Program of Mental Health Research: Each of these contemplated studies is aimed toward the clarification of the role of a perceptual function in determining behavior or toward a delineation of the determinants of a particular perceptual process. In the present size-constancy problem some evidence would indicate that rationalizing individuals or individuals with paranoid-like tendencies should manifest a greater discrepancy between their responses under instruction I and II. In addition to determining whether such an hypothesis is correct, the present approach is oriented toward the very much more important theoretical issue of whether such a finding should be interpreted as a perceptual phenomenon or as a judgmental or performance phenomenon. Much of the character of human behavior is often attributed to perceptual processes, but there exists very little experimental evidence which really supports this viewpoint unequivocally.
Part A. Project Description Sheet Continued

Proposed Course of Project: This project is conceived as an indefinitely continuing one in which normal control data relevant to other projects is obtained.

Part B included: No
Project Title: Environmental and Genetic Modification of Biological Systems.

Principal Investigator: John D. Calhoun

Other Investigators: William D. Skinner

Cooperating Units: Area 1 of this project includes the census taking of small mammals in their native habitat. Many of these are potential reservoir hosts of diseases transmittable to man. What we are doing in this program should be of relevance to certain activities of the Rocky Mountain Laboratory and the Communicable Disease Center.

Man Years
Total: 216 2/3%
Professional: 100%
Other: Research Assistant: 100%
Secretarial: 16 2/3%

Project Description:

Objectives: To gain insight into the ability of animals to adjust to conditions over which they have little or no control. The ultimate aim is to develop principles of structuring the physical and social environment enabling optimum adjustment with respect to genetically determined capacities. In the realization of these objectives emphasis is given to the use of space through time by socially organized
Objectives continued: groups in complex environments. Where single individuals or small groups are utilized in highly simplified and controlled experimental conditions, these experiments are considered not as ends of themselves, but as means toward a fuller appreciation of the processes characteristic of organized groups in complex situations.

Methods Employed: Wild and domesticated strains of rodents as subjects. These fall into three areas:

Area 1. Population dynamics of vertebrates living under natural conditions. This is a cooperative endeavour in which the major investigator coordinates the activities of a number of investigators over North America who utilize standardized procedures for sampling populations of small mammals.

Area 2. Short term experimental studies.

a. Physiological and behavioral consequences of group formation in mice. Groups 1, 2, 4, 8, 16 and 32 were given ten 2-hour sessions in a 24 x 27 inch field composed of seventy-two 3-inch square compartments with doors on each side. All mice were marked and time lapse photography was conducted on each session. Mice were killed and preserved for later study at the end of the 10th session.

b. Utilization of space through time by rats in the activity alley. The alley is an 8 inch wide 14 foot enclosure with a nest compartment at one end. Many different groups of rats have been given 24 to 72 hour sessions individually in this apparatus during the past three years. We are now in the process of analyzing the results.

Area 3. Consequences of long term experience in differentially structured environments. This area of the project is now being set up at the Rockville Farm Barn. A wild and a domesticated strain of rat will be reared in each of four environments.

a. Minimum environment. Isolation of single individuals in cages of 0.19 cu. ft. which permits few perceptions or activities.
Part A. Project Description Sheet Continued

Methods Employed Continued:

b. Moderate environment. Life space cage. This 6 cu. ft. cage is so designed as to permit most basic behaviors. One male, two females, and their unweaned young will comprise the group.

c. Positive environment. One-thousand two-hundred and sixty cu. ft. cage structured to foster tolerance and social integration. Group will be maintained at approximately 60 rats.

d. Negative environment. One-thousand two-hundred and sixty cu. ft. cage structured to foster intolerance and lack of social organization. Groups will be maintained at approximately 60 rats.

An observational record will be maintained regarding the behavior and biology of numbers of each group in situ. Representatives of five age groups will be permanently removed to serve as "clinical" subjects upon whom an assessment will be prepared of their behavioral capacities, physiological state, and pathological picture.

Major Findings:

Area 1. Population dynamics of vertebrates living under natural conditions. The analysis of two field studies relating to mice and shrews living in woodlands revealed that the several species forming the community express a social hierarchy in their utilization of space. Members of the dominant species have relatively large home ranges and maximize distance between centers of home ranges. Members of the next most dominant species have smaller home ranges and each of these individuals maximizes his distance from members of his own species as well as from individuals of the most dominant species. This process continues down the hierarchy until the most subordinate species is highly cryptic in the sense that its members have very small home ranges and each member maximizes its distance not only from its own kind but from that of members of all higher ranking species. When such populations are subjected to removal, trapping the dominant species is removed first since it has the highest probability of exposure to traps. As it is removed the members of each of the subordinate species begins to enlarge.
Part A. Project Description Sheet Continued

Major Findings continued: its home range such that their probability of capture increases. As a result of this process the lower a species stands in the community hierarchy the later in time is the maximum catch per day. This concept is substantiated by the results of a nine-year cooperative study coordinated by Calhoun in which the data on 20,000 small mammals trapped in the field have been supplied him.

Area 2. Utilization of space through time by rats in the activity alley. Analysis of the first study in this area has been completed. For each of four behaviors their frequency as a function of their duration is describable by negative exponential curves. Each behavior is characterized by a specific equation differing from that of the other behaviors. Furthermore, the duration of any particular behavior is independent of the duration of the preceding or following behavior of the same or different kind. The frequency with which trips are terminated from a starting point is described by a K/distance relationship in which K is approximately 0.9.

Area 3. Consequences of long term experience in differentially structured environments. See 1956 annual report for details of these environments. No studies are yet in progress in this area. The end of 1957 will see the completion of the laboratory at the Rockville Farm Barn which will enable initiation of the studies.

Significance to the Program of Mental Health Research: Most animals, including man, live in environments over which they actually have little control with respect to their life span. That is many characteristics of the environment are extremely stable. If this project is successful in defining principles by which behavior is modified by the static components of the environment, it should be possible to extrapolate these principles to other forms so that a more optimum environment may be striven for.

Proposed Course of Project:

Area 1. The results of the past several years cooperative field studies of small mammals have been typed for lithoprinting as an administrative publication. As soon as these are distributed to the cooperators, both Calhoun and some of the other cooperators will then be in the position to analyze and publish results. It is
Proposed Course of Project continued: already apparent that these biological "particles", small mammals, exhibit many characteristics similar to the behavior of gas molecules. It is our objective to define the relevant principles of social physics. We do not know how far up the animal kingdom toward man these principles will apply. However, we believe that these studies are not without relevance since the equations describing the physics of the movement of an individual within its own home range have been found to adequately describe the distribution of members about an institution exemplified by a church in a recent pilot study by Calhoun.

Area 2. With the result of the first study now analyzed as a guide we hope during 1957 to make progress in analyzing related studies of rats in the activity alley in which either the emotional past history of the rats was varied or in which the alley was structured with various stimulus situations. Gross inspection of the records reveals that both of these types of variables alters the utilization of space and time. With regard to further studies a major change has been made in the apparatus. This concerns doubling the length of the alley to 28 feet and speeding up the flow of recorder paper by five times. Thus, we will be able to analyze the time aspects of behavior with ten times the prior accuracy. The initial studies with the activity alley have lead to the hypothesis that the utilization of space and time is a consequence of the amplitude and frequency of discharges from the reticular activating system of the brain stem. We therefore propose to modify the rat's physiology through the use of certain drugs or emotional conditioning processes which should affect the function of the brain stem and, therefore, the behavior of the rat in the activity alley.

Area 3. The entire year 1958 will be devoted to pilot studies. Groups of rats will be raised in each of the four experimental environments. Observational procedures will be standardized and the various behavioral testing equipment constructed and calibrated.
Part B. Honors, Awards, and Publications


Calhoun, John B. Editor, *Proceedings of Conferences on Environmental Determinants of Mental Health*. Part I, 130 pages; Part II, 191 pages. These proceedings were prepared as Colitho reproductions in a limited supply for the use by the consultants invited to participate by the National Institute of Mental Health at these two conferences held in May and October 1956.

Honors and Awards relating to the project: None
NATIONAL INSTITUTE OF MENTAL HEALTH

Basic Research
Laboratory of Socio-environmental Studies
Office of the Chief

BUDGET SHEET

Estimated Obligations for FY 1958

Total: $16,571
Direct: $12,732
Reimbursements: $3,839

Projects included: M-S-C 1 through M-S-C 3
Part A.

Project Title: Analysis of Theoretical and Methodological Issues in the Sociology of Mental Health and Illness

Principal Investigator: John A. Clausen

Other Investigators: None

Cooperating Units: None

Man Years (calendar year 1957): Professional: 1/3
Other: 2/3

Patient Days (calendar year 1957): None

Project Description:

Objectives: To examine current research within the Laboratory and within the larger field, searching for theoretical convergences and for problematic issues in the empirical findings, especially bearing upon the relationship between social structure and personality development.

Methods Employed: Collection of theoretical formulations and research findings on the relationship of social and cultural factors to aspects or dimensions of mental health in various communities, population groups or cultures, as a basis for scrutinizing theoretical linkages, convergences or critical discrepancies and developing more incisive and more rigorously testable formulations. Specifically, investigation thus far has involved studies of narcotics use among adolescents and young adults (bringing together psychiatric, psychological and sociological data derived from several decades of research in a variety of communities in an effort to develop an integrated frame of reference for the understanding of narcotics use in the urban slum) and studies of the early family experience of schizophrenics (examining especially ecological studies and studies dealing with the dynamics of interpersonal relationships in the family of the patient).

Major Findings: In both areas of pathology analyzed thus far, it appears that the social matrix in which the deviant develops and his expressions of pathology (as viewed by clinicians) tend
to interact and to produce correlations which are frequently but incorrectly interpreted as evidence of etiological linkage. The contradicting findings of studies in different communities of the distribution of schizophrenia by social class and by social mobility groupings likewise suggest that correlations may represent sifting processes rather than causal nexuses.

A variety of formulations which attribute to the mother a "schizophrenogenic" role appear to rest in large part upon lack of adequate controls and upon failure to analyze adequately the selective biases entailed when a limited number of families of long-chronic schizophrenics participate in therapy.

Significance to Mental Health Research: A great many inconclusive studies have been attempted in premature efforts to "establish" causal relationships between social factors, especially family dynamics, and specific pathologies. An analysis of the reasons for inconclusiveness and of the implications of studies which support or contradict each other, including our research gives a basis for planning a series of limited strategic studies to eliminate some of the alternative hypotheses which would "explain" observed correlations.

Proposed Course of Project: This program of research surveillance will be more or less continuous. During the coming months a major formulation on the status of research on family relations and schizophrenia will be prepared for publication and several research possibilities investigated.

Part B included Yes \[\checkmark\]  No \[\_\_]
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:

Clausen, John A., "The Ecology of Mental Illness," Presented at the Symposium on Social and Preventive Psychiatry, Walter Reed Army Medical Center, and to be published in the report of the Symposium.


Honors and Awards relating to this project:
ART A.

Project Title: The Impact of Mental Illness Upon the Family

Principal Investigators: John A. Clausen and Leila C. Deasy

Other Investigators: Harriet S. Murphy and Eleanor Carroll

Cooperating Units: Saint Elizabeths Hospital, Washington, D.C. and Springfield State Hospital, Sykesville, Maryland

Man Years (calendar year 1957): Professional: 1-17/30
                                        Other: 1-13/30

Project Description:

Objectives: To study the effects upon the family of the father's or mother's mental illness, by focusing on a limited number of hypotheses and questions raised by an earlier study, within the following areas: (1) the effects of mental illness upon the personal relationships within the family and the family organization, (2) the family's understanding and perspectives of the illness, and (3) the social implications of the illness. Families under study are to include both parental and conjugal families of schizophrenic patients.

Methods Employed: The data are obtained through two structured interviews scheduled shortly after the patient's admission to the hospital and a third interview after several months of hospitalization. The respondents are spouses or parents of schizophrenic patients who are first admissions to the mental hospital. A sample of families of approximately 50 female patients and 50 male patients is planned.

Major Findings: No new substantive findings are ready for reporting.

Significance to Mental Health Research: This study provides data relating to needs in public education regarding mental illness, to the kinds of help needed by the families of patients and to the kinds of social and psychological problems for patient and family attendant to hospitalization of a mental patient.
Part A. (cont.)

Proposed Course of Project: Development of data-gathering instruments and of codes for the analysis of data has been completed, and data-collection on new cases has been resumed. At present 60 of the anticipated 100 cases are in the series. Field work probably will run another year.

Part B included Yes [x] No [ ]
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:


Honors and Awards relating to this project:
Part A.

Project Title: The Adaptation of the Mental Patient to his Family Upon Return from Hospitalization

Principal Investigators: John A. Clausen and Leila G. Deasy

Other Investigators: Harriet S. Murphy

Cooperating Units: Saint Elizabeths Hospital, Washington, D.C. and Springfield State Hospital, Sykesville, Maryland

Man Years (calendar year 1957): None

Patient Days (calendar year 1957): None

Project Description:

Objectives: To study the rehabilitation process following the patient's discharge from a mental hospital, in terms of two interdependent sets of dimensions: (a) the patient's progress toward mental health, and (b) the changing structure and functioning of the family of the patient.

Methods Employed: Patients and families are the same as those studied in project N-S-C-2 and certain of the data secured for that project will be basic to the present project. Data are obtained through interviews with the patient and the patient's spouse or parents and with selected significant others in the patient's social environment. The period of follow-up varies, though for all patients there will be assessments or status reports as of one month, six months and one year after leaving the hospital. Some patients studied in the early phase of data collection will have three to four years of follow-up; patients obtained in the late phase will have one year of follow-up. Additional data come from hospital case reports, psychiatric evaluations of patient's condition at discharge and the investigator's observational ratings of family and patient.

Major Findings: No analyses have been undertaken beyond those reported in 1955.
Significance to Mental Health Research: The high readmission rate of patients to mental hospitals points to the need for research into the factors influencing the discharged patient's adjustment to the family and the community. The present study will add knowledge concerning the kinds of stresses and problems encountered in the process of rehabilitation, and the relationships between conditions in the patient-family-community situation and successful and unsuccessful rehabilitation.

Proposed Course of Project: Field work on this project has awaited the progression of cases in Project M-S-C-2 to the point of discharge of patients from the hospital. In addition to cases currently being carried in Project M-S-C-2, interviews with families who were seen in the initial phase of the project (4 - 5 years ago) will be interviewed in order to explore the long-range effects of the patient's first hospitalization and the subsequent course of family experiences. Field work will probably run another two years.
Basic Research
Laboratory of Socio-environmental Studies
Social Developmental and Family Studies

BUDGET SHEET

Estimated Obligations for FY 1953

Total: $102,108
Direct: $65,307
Reimbursements: $36,801

Projects included: M-S-D 1 through M-S-D 7
**Part A.**

**Project Title:** The Formation of Children's Peer Relationships

**Principal Investigators:** Marian Radke Yarrow and John D. Campbell

**Other Investigators:** None

**Cooperating Units:** Family and Child Services, Washington, D. C.

**Man Years (calendar year 1957):**
- Total: 2-1/4
- Professional: 3/4
- Other: 1-1/2

**Patient Days (calendar year 1957):** None

**Project Description:**

**Objectives:** To investigate the process by which children form impressions of each other and develop patterns of interactions in social situations. To study the effects of developmental, personality and social factors on this process.

**Methods Employed:** Two hundred sixty-seven white and Negro children, 8 to 13 years of age, were interviewed and observed in summer camps, in initial interactions with one another and over a two-week period. Using open-ended, sociometric, and projective questions, interviewers obtained children's impressions and judgments regarding their peers, their adult leaders, and their images of self. Detailed observations of behavior were recorded at selected time periods.

**Major Findings:** (1) A marked degree of sensitivity and reality concerning the characteristics and potentialities of their peers is reflected in the impressions and evaluations reported by children about their peers. Their reports show pronounced agreement with adult assessments and with behavioral records.

(2) Children's initial and almost immediate predictions of the degree of interpersonal attraction which each of their peers will have for them show high agreement with the attraction and rejection developed over a continued period of acquaintance.
(3) In group situations involving increased uncertainties and ambiguities as to interpersonal relations, children's perceptions of one another reflect increased alertness to the "threatening" aspects of interaction and of group roles, i.e., increased sensitivity to aggressive, disruptive and domineering components of others' behavior.

(4) Comparisons of interpersonal perceptions and behavior in racially segregated children's groups with racially integrated groups show that the psychological environment is altered by integration for children without prior experience in mixed groups, but that overt behavior conforms overwhelmingly to the requirements of the equal-status situation.

(5) Negro children respond to integrated groups by increased concern about control of behavior in themselves and peers of their own race. Continued successful interaction in the mixed groups brings some decrease in self-rejection and anxious self-control in the Negro children. Girls' integrated groups appear to have greater difficulties (more tensions and cleavages) than boys' groups, the Negro girl having the lowest status and most negative self-appraisal. These sex differences may be related to differences in adult racial roles of each sex group.

**Significance to Mental Health Research:** A primary concern of parents and professionals working with children is how children's behavior and values are affected by various interpersonal influences of peers and adults and how desired patterns of behavior can be developed. Answers to these questions rest in part on fuller knowledge of the child's interpersonal relationships as he experiences them, i.e., his awareness of others and his sensitivity regarding the behavior and motives of those with whom he interacts.

**Proposed Course of Project:** One aspect of this project's progress during 1957 has been methodological. Techniques for analyzing behavioral and cognitive data within the same conceptual framework have been devised and used in interpreting research results. Publication of research findings has begun. A report on interpersonal dynamics in racial integration has been completed and is in press. A more comprehensive analysis and interpretation of the data on integration is continuing and has been scheduled for publication as a monograph next spring.
Another report is in preparation on factors in interpersonal attraction and rejection in children's groups. It is estimated that the above reports will be completed and additional research papers will be prepared during the next calendar year.
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:


Honors and Awards relating to this project:
Part A.

Project Title: Adult Leadership in Children's Groups: A Study of Leader's Sensitivity and Functioning in Relation to the Social-cultural Composition of the Group

Principal Investigators: Marian Radke Yarrow and John D. Campbell

Other Investigators: Leon Yarrow and John Theban (Not NIH employees)

Cooperating Units: Family and Child Services, Washington, D.C.

Man Years (calendar year 1957):
   Total: 1
   Professional: 1/2
   Other: 1/2

Patient Days (calendar year 1957):

Project Description:

Objectives: To study the adult leader's role in children's groups, assessing: (a) congruencies and discrepancies in leaders' and children's perceptions of interpersonal processes in the group, (b) bases and consequences of discrepancies between leaders' and children's perceptions, and (c) leaders' behavior and sensitivities regarding the individual child and the group in relation to the social class and racial composition of the group.

Methods Employed: Data were obtained on 30 leaders of children's groups and the children in their groups. Each adult led four groups of children (8 per group) in four successive, two-week summer camp sessions. Eight counselors and their cabin groups were studied intensively. Interviews with the counselor, ratings of the children by the counselor, observational records on children and counselor and interviews with the children were obtained. These provided data on leaders' functioning in groups, leaders' perceptions of the attitudes toward the children and children's responses toward each other and toward their leaders.

Major Findings: Analysis has not been completed. Some preliminary findings are as follows:
   1. Adult leaders' appraisals of children tend to be in
agreement with those made by the children themselves. Children rated high in popularity, leadership, etc., by the counselors are in general similarly evaluated by their peers.

2. The leader's personal values and motivations do, however, shape his appraisal of the children. For example, leaders of racially integrated children's groups show a systematic tendency to rate children racially different from themselves higher than children of their own race on socially valued characteristics. Some awareness of this tendency is shown by the children.

3. Adult leaders functioning for the first time in racially integrated children's groups exert tighter control over these groups than they did in segregation. This has been interpreted as stemming in part from their motivation for integration to succeed and in part from their anxiety about the nature of the situation.

Significance to Mental Health Research: Research and theory in personality, developmental and social psychology emphasize the importance of adult influences in shaping children's attitudes and patterns of behavior. With the exception of his parents, a child's teachers are the adults most likely to play a significant role in his development. Application of the data of this project can be made in the field of education.

(a) A recognized problem in many educational settings concerns difficulties arising from differences between teacher and children in cultural and racial backgrounds. Data from this study should identify some of the consequences of these differences in leader-child interactions.

(b) Teachers are faced with the problem of coping with the deviant or the emotionally disturbed child. This study should provide data on the ways in which the adult leader defines deviant behavior to himself and to the children in his group, and on the adequacy of alternative methods used by adult leaders in dealing with the deviant child.

(c) Also, data comparing adult and child perspectives have direct bearing on questions of research methodology in the field of child development; namely, what kind of data source is the adult informant on children's interpersonal relationships.

Proposed Course of Project: Progress on this study is closely linked to the related research project on children's peer relationships. Some of the research findings on the role of the adult leader have been included in the paper on interpersonal dynamics in
Part A (cont.)

racial integration (in press), and these data will be more fully dealt with in a chapter of a report to be published in the Journal of Social Issues in 1958.

During the coming year comparison of adult leaders' and children's perceptions of the personality and social interaction characteristics will continue. Differences in patterns of adult-child relationships and their relations to social and psychological characteristics of the participants will also be explored. It is estimated that data analysis will be completed in the coming year, and final research reports should be ready for publication shortly thereafter.
Part A.

Project Title: The Validity of Retrospective Data on Parent-Child Relationships

Principal Investigators: Marian Radke Yarrow and John D. Campbell

Other Investigators: None

Cooperating Units: National Child Research Center, Washington, D. C.

Man Years (calendar year 1957): Patient Days (calendar year 1957)

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<th>Total</th>
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<tr>
<td>Professional</td>
<td>1/4</td>
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<tr>
<td>Other</td>
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Project Description:

Objectives: To study the extent to which valid information about early aspects of a child's development and parent-child relationships can be obtained from parents' retrospective reports. Specifically: (1) To assess the nature of differences between earlier events and parents' recollection of such events. (2) To determine how retrospection is influenced by such factors as the time interval between events and recall, intervening events, and the current social-psychological situation.

Methods Employed: Parents of children on whom data were obtained from one to 20 years ago will be interviewed. The baseline data consist of direct observations, interviews and ratings of the child and of parent-child relationships gathered at an earlier time concerning the same time period. Parents' retrospective reports will be compared with these baseline data.

Major Findings: Work on this project has not progressed to the stage of data analysis.

Significance to Mental Health Research: This study is basically a methodological one furthering understanding of the process of recall. Research on child development and the etiology of personality disturbances relies heavily on retrospectively reported life-history data. Systematic survey of the accuracy
of such information is necessary to buttress data interpretation and formulation of theory. Thus, study of the nature and extent of systematic errors or biases in retrospective reports on earlier life periods can contribute to the understanding of social developmental factors in the genesis of schizophrenia, delinquent behavior, etc.

Proposed Course of Project: A principal source of baseline data has been located and the major task of abstracting such case-record data has just gotten underway. Development of an interview schedule is proceeding. Interviewing to obtain retrospective reports will begin early in the next calendar year. Two possible extensions of this study are being explored:

(1) Locating and utilizing other existing sources of case-record data to provide baseline information in areas not covered by our present data sources.

(2) Obtaining on-the-spot observational records of nursery school children's interaction with their peers, teachers, and parents, supplementing these observations with interview data, and using the information thus obtained as the baseline for comparison of subsequent retrospective accounts.
Part A.

Project Title: Life-styles in Aging

Principal Investigators: Marian Radke Yarrow and Olive Westbrooke Quinn

Other Investigators: E. Grant Youmans

Cooperating Units: Laboratory of Clinical Sciences, Laboratory of Psychology, and Social Service Department, NIH.

Man Years (calendar year 1957): 
Total: 1-1/2
Professional: 1-1/4
Other: 1/4

Patient Days (calendar year 1957): 55

Project Description:

Objectives: This project is part of a larger research on the functioning of physically healthy aged persons, which brings the perspectives and measurements of physiology, psychiatry, psychology, and sociology, both singly and in combination, to the examination of the problems and factors in aging. The primary objective of this part of the total research is to examine relationships between the demands and supports of the aged person's social environment and his functioning—as it is defined in terms of the organization of his daily behavior, his planning for the future, his attitudes toward himself and his relationships with others. Environment is assessed in terms of (1) the social expectations and stereotypes imposed upon old age, and (2) the impact of common changes or crises of old age, such as retirement from employment, family losses, and social isolations.

A second research objective is the investigation of interrelationships between the social psychological variables described above and physiological, psychiatric, perceptual and cognitive data.

Methods Employed: Physically healthy male subjects were brought to the Clinical Center for two weeks of intensive study by investigators from several cooperating Laboratories. For the social psychological study within the
larger interdisciplinary project, data are obtained through a series of interviews, two of which are conducted while the subject is living at the Clinical Center, a third with the subject in his home about a month later and a fourth with a person chosen by the subject who has known him over a long period of time. In addition, systematic observations of the subjects are made by the nursing staff on the Ward and by a sample of the investigators.

**Major Findings:** Preliminary analyses suggest:

1. A stable structure of interpersonal relationships is important for adequate functioning in old age. Extensive losses suffered by the aging individual, through death of or abandonments by persons significant to him, are associated with (a) daily behavior which is less organized, more routine-bound and lacking in goal character, (b) a lack of goals and emotional investments beyond the self, and (c) an inability to use or to enjoy leisure time on the part of the aging individual.

2. Elderly persons in our society are measured by others by the yardstick of youth. The respect accorded them is related to the extent to which they depart from the stereotype of the aged person, a stereotype deriving from the characteristics of sick elderly persons. Many common social expectations as to what elderly persons can or should be allowed to do are based on this stereotype, which to some degree does not fit the physically healthy group of aged studied here.

3. Our data do not support the popular belief that problems of retirement are most ably handled by persons of higher educational or professional training. Occupational background, per se, shows no systematic relationship to ability to cope with problems of old age.

4. Relationships between physiological measures and social functioning are being explored. One such relationship appears in preliminary analysis. Persons who have suffered the greatest personal losses (see 1 above) and who are at the low extreme in measures of \( O_2 \) consumption show the greatest impoverishments in daily behavior and goal striving, and the inverse of the case holds equally. Causal inferences cannot be drawn from present data of co-variation.

**Significance to Mental Health Research:** Ours is a population in which the proportion of elderly people is steadily increasing. Many groups (medicine, social work, and other community services) which deal with problems of old age and which seek to make old age a more satisfying and productive time of life need the kind of
information this project seeks, in order that they may plan their services to meet needs of the aged. In this respect it is especially important that research data be obtained on a non-institutionalized population. We expect this research to contribute to the understanding of the following questions:

(a) What demands and/or pressures relate to adequate functioning of the aged person in the community?
(b) What relationships are there between social-psychological factors and physiological factors in aging?
(c) What does it mean to elderly people to grow old, and what is the meaning of aging to younger individuals? What elements of difference between the concepts of aging for older and younger people are conducive to strain?
(d) What social factors in the individual's daily living are associated with his adjustment to aging?

Proposed Course of Project: Data gathering was completed in the summer of 1957. Analysis of the data is underway. A paper will be ready for publication during the next year.
Part A.

Project Title: The Identification of Self in Identical Quadruplets: A Special Case of the Problems of Sibling Rivalry and of Multiple Status

Principal Investigators: Olive Westbrooke Quinn

Other Investigators: None

Cooperating Units: None

Man Years (calendar year 1957): 2/3

Professional: 1/3

Other: 1/3

Patient Days (calendar year 1957): 190

Project Description:

Objectives: To analyze (1) interactional patterns, and (2) incompatible statuses in a group of mentally ill identical quadruplets, in an effort to understand the individual's struggle to establish a definition of self in relation to the group. This problem is seen within the framework of stresses arising from or exaggerated by the fact of multiple birth.

Methods Employed: The subjects are schizophrenic identical quadruplets under the care of the Clinical Investigations Branch of NIMH. Within the clinical setting data have been collected by means of observations of the patients; informal interviews with the patients and with nurses and attendants, and observations of and informal interviews with the parents upon the occasions of their visits here. From the home community there are interviews with friends, neighbors, teachers, and others in a position to tell how these patients and their family are perceived by the community in which they lived. In addition, the personal and public documents concerning the subjects have been used.

Major Findings: Problems of self-identification apparently unique to or exaggerated by the fact of multiple birth seem to arise from a conflict of two opposing kinds of pressures: (1) pressures upon the persons of the multiple set to
occupy a single position and (2) pressures upon the members of a set defined as "identical" to exhibit distinctive differences. The interplay of these pressures is such that individuality is defined in reference to the other members of the set. There is an intermediate zone between seeing oneself as an indistinguishable part of a whole and seeing oneself as a unique individual (or being seen in either of these ways by others). Sub-groupings and coalitions within the set occur; i.e., a pair or trio distinguishes itself from another pair or singleton with respect to a given trait. These sub-groupings change as the trait under consideration changes.

The process by which others have kept the quadruplets "identical" in their own thinking is one in which some very obvious and large early differences were ignored or explained away as temporary, something the individual would outgrow. On the other hand, the necessity for distinguishing individual members of the set gave rise to an opposing process. Initially small or negligible differences have been seized upon and exaggerated, and in their exaggerated form have become the basis for evaluation of the individual and for interaction with her.

**Significance to Mental Health Research:** Certain problems of child development and child rearing which arise in the family group are exaggerated by the fact of multiple birth and are therefore more readily accessible to study and to analysis. The central problem of this project, that of the development of identification of self, is here placed in the special setting of multiple birth.

**Proposed Course of Project:** A report is in preparation, directed toward answering the following questions: When two or more persons are defined as "identical," how do they and those who must interact with them establish the identities of each? How is the individual's identity determined by his similarities to others in the multiple set, and how does it rest on perceived differences?

Part B included  Yes [ ]  No [x]  - 479 -
Part A.

Project Title: The "X" Family as Seen by the Community

Principal Investigator: Olive Westbrooke Quinn

Other Investigators: Leila Calhoun Deasy

Cooperating Units: None

Man Years (calendar year 1957): Patient Days (calendar year 1957):
    Total: 1
    Professional: 2/3
    Other: 1/3
    none

Project Description:

Objectives: This is one part of a larger study of the "X" family from the points of view of various disciplines, with the intent of deriving or exemplifying hypotheses regarding nature-nurture contributions to the development of schizophrenia. In this regard, the influences of the family on the community and of the community on the family comprise an area of information essential to a full understanding of how mental illness in the "X" quadruplets developed.

Methods Employed: Interviews were conducted with the friends, relatives, teachers, doctors, employers, work associates, neighbors, and certain individuals who had assumed some sponsorship of the subjects. Data include observations of parental interaction in their home, hospital and clinic records, and interviews with 76 informants. Information was obtained on (a) patterns of behavior within the family and (b) community attitudes toward the family.

Major Findings: Analysis is in progress. No findings can be reported at this time.

Significance to Mental Health Research: Much mental disorder is believed to stem from unhealthy family relationships. Any effective program of prevention of mental illness would have to take into account the circumstances which contribute to the autonomy of parents in rearing their children.
Proposed Course of Project: Analysis in progress focusses on family autonomy in child-rearing practices, with special reference to the problem of access to pathogenic families. How early and by what means is such a family detected in the community? Under what circumstances and through what avenues can community members influence the parents to alter their conduct toward their children?
Part A.

Project Title: Exploratory Study of Methodology for Assessing Interpersonal Relationships Within the Family

Principal Investigators: Marian Radke Yarrow and Thomas Gillette

Other Investigators: None

Cooperating Units: None

Man Years (calendar year 1957): 1/2
Professional: 1/2
Other: -

Project Description:

Objectives: To develop techniques of investigating interpersonal relationships within the family, in the natural family setting.

Methods Employed: This research is primarily methodological. It proposes to develop methods of studying the family in its natural setting, as compared with laboratory, testing or interviewing settings. It will be necessary to work through problems deriving from the nature of this setting, problems of observation and recording, problems of conceptualization and ethical problems.

Major Findings: Not applicable. Project in planning stage.

Significance to Mental Health Research: The fundamental importance of the family in influencing development is well recognized. Most research on the family, however, uses data derived from second-hand sources. The orthodox techniques have been case histories, personal interviews and questionnaires. Rarely are data obtained from direct observations of intra-familial interaction. It is assumed that new sensitivities and insights regarding family characteristics and interactions may be developed if methods of obtaining first hand data can be worked out. Such findings would be significant for many areas of child development and family research.
Proposed Course of Project: The past several months have been spent in assembling methodological leads from the research literature and in drawing up tentative plans for testing a number of observational approaches. This work will continue. During the next year a more definite project formulation will be developed. It will be regarded as exploratory research, methodologically, but will attempt at the same time to obtain substantive data on the problem of multiple-mothering.
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:


Honors and Awards relating to this project:
Basic Research
Laboratory of Socio-environmental Studies
Community and Population Studies

BUDGET SHEET

Estimated Obligations for FY 1958

Total: $96,575
Direct: $74,222
Reimbursements: $22,353

Projects included: M-S-P 1 through M-S-P 5
Part A.

Project Title: A Comparison of the Social Relationships of Children in the Middle and Lower Socio-economic Strata

Principal Investigators: Melvin L. Kohn and John A. Clausen

Other Investigators: Eleanor Carroll

Cooperating Units: None

Man Years (calendar year 1957): Patient Days (calendar year 1957)
- Total 2-9/10
- Professional 1-3/5
- Other 2-3/10
None

Project Description:

Objectives: To ascertain whether or not there are consistent and patterned differences between the social relationships of children from the middle and lower socio-economic strata of urban society.

Methods Employed: Structured interviews with a sample of middle and lower socio-economic status parents of 9-10 year old children, together with interviews with a sub-sample of the children themselves. The interview schedule for parents has been designed to illumine the several dimensions of the parent-child relationships, the values of the parents most relevant to their behavior as parents, their evaluations of their children's behavior, and their knowledge and structuring of their children's relations with other children. The interview schedule for the children has been designed to elicit their perceptions of their relations with their parents, as well as a more complete picture of their relationships with other children.

Major Findings: The first portion of data-analysis has been a comparison of the values of middle and working class parents. It was found that parents in the two classes share a common value-system with respect to what characteristics they consider most desirable in a child of this age: they ascribe predominant importance to items connoting character and to happiness; they are

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not likely to value physical prowess, seriousness, ability to play by oneself or affective responsiveness very highly for children of this age. But happiness is no. highly valued by nearly as large a proportion of working class as of middle class parents. And, although items connoting character are of primary importance to parents of both classes, middle class parents are more likely to value both self-control and consideration, working class parents to value obedience. Furthermore, middle class mothers are considerably more likely to regard curiosity as a prime virtue, whereas working class mothers value neatness and cleanliness.

The study also demonstrates that the values parents hold are closely related to the ways that they raise their children.

**Significance to Mental Health Research:** One plausible interpretation of the disproportionately high rates of schizophrenia in the lower socio-economic strata is that the childhood social experiences of persons from these strata have predisposed them to illness. Though plausible, this interpretation does not get us very far in our understanding of schizophrenic personality development until we are able to specify in detail the respects in which the childhood social relations of these persons differ from those of other groups in the society. This knowledge we seek to secure in the present research. We hope that the results of the study will make possible the formulation of more penetrating hypotheses about the role of social experience in the development of schizophrenia than those that have been produced to date.

**Proposed Course of Project:** By the beginning of 1957, the interviews with the sample of 300 mothers had been completed, as were nearly one-half of those in families where mother, father, and child were to be interviewed. During 1957 the remaining interviews, the processing of interview materials for IBM punching and the first stage of data analysis—a comparison of the values of lower and middle socio-economic status parents—were completed. During 1958 data analysis will be continued; the emphasis will now shift to a direct examination of the several dimensions of family interaction.
Part A.

Project Title: Exploratory Study of the Use of Local Community Resources for Handling Mental Health Problems

Principal Investigator: Stephen T. Boggs

Other Investigators: None

Cooperating Units: Program Development Branch, Bureau of State Services, Public Health Service

Man Years (calendar year 1957): 1

Patient Days (calendar year 1957): None

Project Description:

Objectives: To evolve and test hypotheses about the utilization of formal agencies and informal resources (family, friends, associates, and strangers) by people with personal problems; the social factors in the community affecting this utilization; and the consequences of various ways of handling problems for the subsequent career of the individual.

Methods Employed: In the exploratory phase previous studies of social class differences in individual relationships with social and psychiatric service agencies, popular conceptions of mental illness, and of the places people take their troubles have been reviewed. Twenty-four trial interviews were conducted in a rural community on the Great Plains as part of a collaborative study undertaken with the Program Development Branch, Bureau of State Services, Public Health Service. The development of a systematic design for testing the hypotheses is now underway.

Major Findings: A number of hypotheses have been evolved and revised.

These stress the importance of informal resources, social class and rural-urban differences in readiness to utilize these resources effectively, and the impact this may have on the career of the troubled individual and those around him.
Significance to Mental Health Research: It may prove possible to elucidate individual social reactions to normal stress and, eventually, to differentiate these from the careers which predispose to hospitalization within certain social settings.

Proposed Course of Project: With exploratory work complete, the project will be ready for systematic collection of data and testing of hypotheses during the calendar year 1958.
Part A.

Project Title: Pre-hospital Social Factors, Treatment with the Tranquilizing Drugs, and Behavior as Prognosticators of Successful Release from a Mental Hospital

Principal Investigator: Erwin L. Linn

Other Investigators: None

Cooperating Units: The staff of Saint Elizabeths Hospital has cooperated in this project by making available hospital records.

Man Years (calendar year 1957): 1-1/4
Patient Days (calendar year 1957): None

Project Description:

Objectives: To determine the relationship between (a) the patient's pre-hospital social background, (b) his course of treatment in the hospital (with particular interest in reserpine and chlorpromazine) and (c) his behavior while in the hospital and the duration of hospitalization and probability of readmission, for functionally psychotic patients. Among the questions to be asked are the following:

1. Are patients treated with chlorpromazine or reserpine more likely to be released during the first year of hospitalization and more likely to remain out of the hospital one year after release than a comparable group of patients admitted to the hospital before the use of tranquilizing drugs?

2. Have the tranquilizing drugs increased the probability of release of patients not treated with drugs because of the generally "calmer" atmosphere of the hospital during the current period of drug therapy?

3. To what extent do patients of varying social backgrounds react differentially to the drugs?

Methods Employed: Abstraction of relevant data from the hospital medical charts, including nurses notes and medication sheets, of all functional psychotics, age 20 through 49,
residents of the District of Columbia for one year or more, who were admitted to Saint Elizabeth's Hospital for the first time during 1/1/53 through 8/31/56. These data have been coded for IBM card preparation and tabulations.

**Major Findings:** Analysis of data not yet begun.

**Significance to Mental Health Research:** The questions enumerated above are central to current interest in factors influencing admission and release from mental hospitals.

**Proposed Course of Project:** During 1957 the project was formulated and the data collected and coded for IBM tabulation. Analysis of data will be carried out during 1958.
Project Title: A Twin Family Study of Mental Deficiency

Principal Investigators: Dr. Franz J. Kallmann (non-PHS) and Dr. Gordon Allen

Other Investigators: (Those previously listed have not participated this year.)

Cooperating Units: New York State Psychiatric Institute

Project Description:

Objectives: To assess the frequency with which mental subnormality can clearly be ascribed to nongenetic factors and to elucidate the interaction of genetic constitution with environmental causes of subnormality. Also to develop better methods for the collection and interpretation of twin data in medical research.

Methods Employed: A reporting system set up in 1937 by Dr. Kallmann provided index information on a large number of mentally subnormal twins in New York State, mainly in the State Schools for Mental Defectives. During the four year period, July 1952 to June 1956, additional information was abstracted from institutional records and obtained on visits to homes and hospitals. Accessible twins were examined, many of them with the aid of x-rays, electroencephalograms, and psychological tests.

Pairs studied in detail were classified as to zygosity. Clinical diagnoses were reviewed in the light of all information obtained. Case studies have been summarized and all essential information is punched on McBee cards for statistical analysis.

Patient Material: The material consists of 585 multiple births represented by 725 index cases. Over 150 pairs have been studied in detail.
Major Findings: The work this year has consisted of reviewing cases and coding data.

Significance to Mental Health Research: The study provides leads for further genetic research in mental defect, and in some instances, like monogolism, it may provide decisive information relevant to existing etiological theories.

Proposed Course of Project: Summarization of cases and coding of data took longer than expected and may continue into 1958. Analysis should be completed during 1958, and publications the following year.
Part B: Honors, Awards, and Publications

Publications other than abstracts from this project:


Other publications:


Honors and Awards relating to this project:

None
Part A.

Project Title: Social Mobility and the Milieu of the Psychiatric Hospital

Principal Investigators: Leslie Schaffer and Leila Calhoun Deasy

Other Investigators: None

Cooperating Units: Adult Psychiatry Branch, M-AP(C)-9.

Man Years (calendar year 1957): Total: 1/3

Patient Days (calendar year 1957): None

Other: -

Project Description:

Described in full by Adult Psychiatry, Project Serial No. M-AP(C)-9.

Part B included Yes ☐ No ☒