

## 600 Participate In Dedication of NIDR Building

The newest building at NIH, and the first which the National Institute of Dental Research could call its own, was dedicated Friday, May 26.

A distinguished assembly of speakers and approximately 600 guests participated in the outdoor ceremonies, sandwiched in between showers.

Dr. Francis A. Arnold, NIDR Director, and Dr. John Knutson, Chief Public Health Service Dental Officer, collaborated as presiding officers.

### Research Parallels Growth

The principal speaker, Dr. Emory Morris, President of the W. K. Kellogg Foundation, pointed to the significant parallel in the evolution of dental research and the growth of the NIDR in scope and influence.

"Only three decades have elapsed since Dr. H. Trendly Dean (first Institute Director) and his dental hygiene unit formed the nucleus of what grew into this now internationally famous Institute," Dr. Morris recalled.

"We in the Kellogg Foundation,"

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## Weatherman and Secretary Cooperate To Assure Good Health at Dedication

The program planned for the dedication of NIDR's new laboratory-office building was held outside as scheduled—thanks to the Weather Bureau's accurate tracking of several thunderstorms that dumped almost an inch of rain on the reservation before and after the ceremonies, timed to begin at 2 p. m.

### Predictions Accurate

The forecasters, consulted by phone, predicted with uncanny accuracy the departure of one storm at 2:05 and the arrival of another at 3 o'clock.

No sooner were the seats wiped dry by the NIH grounds crew than they were filled by the 600 waiting guests, and the program got under way.

## House Allows \$641 Million for NIH, Votes Construction Grant Funds

Under the Labor-HEW appropriations bill as passed by the House, NIH would receive an operating appropriation of \$641 million for fiscal year 1962.

This compares with the President's budget request of \$583 million and last year's final appropriation of \$560 million.

The NIH appropriations are contained in the Public Health Service portion of the bill (H.R. 7035) which allows \$1.12 billion for PHS

in the DHEW appropriation of \$4.02 billion.

The measure was approved by the House as submitted by its Appropriations Subcommittee, chaired by Rep. John E. Fogarty of Rhode Island.

The House further approved a \$30 million appropriation to continue the health research facility program of matching grants for construction, renovation, and equipment of research laboratories at university medical schools and similar health study centers.

### Senate Hearings Begin

The Senate Appropriations Subcommittee, under the chairmanship of Sen. Lister Hill of Alabama, began its hearings on the bill on May 24.

The House action, taken May 17, would make available, under additional appropriations, funds for special grant programs to support the construction of research facilities.

These funds include \$5 million set aside for cancer research facilities and \$10 million earmarked for the construction of hospital research facilities.

Funds for construction at NIH, amounting to \$4.63 million, were approved as part of the PHS Buildings and Facilities appropriation, totaling \$16.6 million.

A breakdown of the House allowance for NIH, exclusive of construction grant funds, follows.

Appropriation	(Millions)
General Research and Services	\$119.3
NCI	125.7
NIMH	92.2
NHI	105.7
NIDR	14.7
NIAMD	73.6
NIAID	52.2
NINDB	57.6
<b>Total</b>	<b>\$641.0</b>



Chatting in front of the new Dental Institute Building prior to the dedication ceremonies are, from left: DHEW Secretary Abraham Ribicoff, Senator Lister Hill of Alabama, and NIH Director James A. Shannon.

## Serious Mycoses Yield to Therapy With New Drug

A new antibiotic derived from an unnamed species of Streptomyces is reported to possess therapeutic value against several of the serious systemic mycoses. Its co-discoverers, Drs. Emanuel Grunberg and Julius Berger, of Hoffman-LaRoche's Chemotherapy Laboratory, assigned the experimental drug a code designation, X-5079C.

Trials in experimental mycoses by Dr. Chester W. Emmons, Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, immediately confirmed the low toxicity and therapeutic activity observed by Drs. Grunberg and Berger.

### Tested Clinically

The drug has been under clinical test since 1958 by Drs. John P. Utz and Vincent T. Andriole, NIAID Laboratory of Clinical Investigation. Results of their study of patients hospitalized at the Clinical Center with a variety of culturally confirmed fungal infections were presented at the recent meeting of the American Thoracic Society.

Four of five patients treated with X-5079C showed dramatic clinical recovery from severe disseminated histoplasmosis. The one failure was questionable since treatment duration was considered too brief for valid evaluation. Three other cases of chronic cavitary histoplasmosis were effectively treated; cultures became negative in these patients.

### Recoveries Are Complete

The drug produced some interference with liver function, but no irreversible damage, so far as present data indicates.

Of six patients who had blastomycosis, including two with osteomyelitis, four apparently made complete recoveries. Two of three patients with sporotrichosis infection severe enough to involve bones and joints were judged cured by treatment with X-5079C. They had shown no response to previous io-

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# the NIH Record

Published bi-weekly at Bethesda, Md., by the Public Information Section, Office of Research Information, for the information of employees of the National Institutes of Health, principal research center of the Public Health Service, U. S. Department of Health, Education, and Welfare.

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## DESIGN CONTRACT AWARDED FOR FIRST ANIMAL FARM BUILDINGS

The Washington firm of Hayes, Seay, Mattern and Mattern was awarded a \$130,095 contract on May 16 by the General Services Administration for the design and planning of the first stage of construction on the NIH Animal Farm.

A farm animal building, a dog and cat kennel with an attached animal hospital facility, and a central power plant and other utilities are to be designed.

### Construction Planned

Under the present planning schedule, construction of these first buildings will start early in the fiscal year 1963. The cost will be an estimated \$2,800,000.

An estimated \$11 million will be spent on the animal farm project by the time all buildings are completed.

The 500-acre animal farm was purchased a year ago to expand animal production facilities and to replace a small farm that NIH had

occupied near Gaithersburg since 1949 and had outgrown by 1959.

During the year that NIH has owned the property, the existing farm buildings have been repaired, temporary kennels have been constructed, and the construction of an animal quarantine building has been started.

### Animals Moved

A small number of dogs have been moved to the farm, and a few cattle, horses, and goats have been pastured there since last fall.

Planning for development of the farm has been handled by the Division of Research Services in cooperation with the Institutes and other Divisions at NIH which will use the buildings.

## Malcolm Rogers Award Won by Dr. Sarnoff For Cardiac Research

Dr. Stanley J. Sarnoff, Chief of the Laboratory of Cardiovascular Physiology of the National Heart Institute, has been named the winner of the 1961 Malcolm Rogers Memorial Award.

The award of \$500, presented annually "for excellence in the field of cardiovascular disease," is endowed by a grateful patient of the late Dr. Malcolm Rogers, a Milwaukee cardiologist.

The award will be presented to Dr. Sarnoff in Milwaukee on June 10. On that date he will deliver the "Annual Memorial Lecture" at the scientific meeting of the Wisconsin Heart Association. Dr. Sarnoff will speak on "Circulatory Regulation" with special reference to cardiac output.

This is the fourth such honor to come to Dr. Sarnoff this year. Earlier he had been named Halliburton Memorial Lecturer by King's College, London; St. Cyres Lecturer by the National Heart Hospital of the Royal Society of Medicine, London; and vice-president of the American College of Cardiology.

A graduate of Princeton and Johns Hopkins Medical School, Dr. Sarnoff has headed the Laboratory of Cardiovascular Physiology since 1954. He came to NHI from the Harvard School of Public Health, where he was Associate Professor of Physiology.

## New Brochure Outlines PSC Grants Programs

The Psychopharmacology Service Center of the National Institute of Mental Health recently announced publication of a folder describing its work.

The folder outlines the Center's research grants program and other types of financial support available for training, teaching, surveys, laboratory construction, and related activities in the field of psychopharmacology.

Established in 1956, the Center has special responsibility for developing a balanced program to support research and facilitate exchange of information in psychopharmacology.

Single copies of the folder, PHS Publication No. 809, may be obtained from the PSC Scientific Information Unit, Bldg. T-6, Rm. 2111, Ext. 5195, or from the NIMH Publications and Reports Section, National Bank Building, Bethesda,

## Two Universities Get Grants for Primate Centers

The Public Health Service has announced two grants totaling \$3,203,544 to the University of Wisconsin and the University of Washington for the construction and operation of two Primate Research Centers.

Construction on both Centers is scheduled to begin in early 1962.

"Primate colonies for research purposes play a key role in the conquest of disease," Surgeon General Terry said. "They provide scientists with unique opportunities for the study of species similar to man both structurally and physiologically.

### Benefits Foreseen

"The Wisconsin and Washington Primate Research Centers," he pointed out, "will make possible long-term studies of great research potential. All sciences concerned with mental and physical disorders in man may some day benefit from the existence of facilities such as these."

When in full operation, the two Centers will provide special environments for research to advance all areas of knowledge on the biological characteristics of non-human primates.

The grant to the Wisconsin Center totals \$1,664,540 for initial operation and construction of a four-story building on the University of Wisconsin campus in Madison.

### Brain Studies Emphasized

Special emphasis will be given to studies concerning the functions of the brain and psychological disorders.

The grant to the Washington Center totals \$1,539,014 for initial operation and construction of new facilities on the campus of the University of Washington in Seattle.

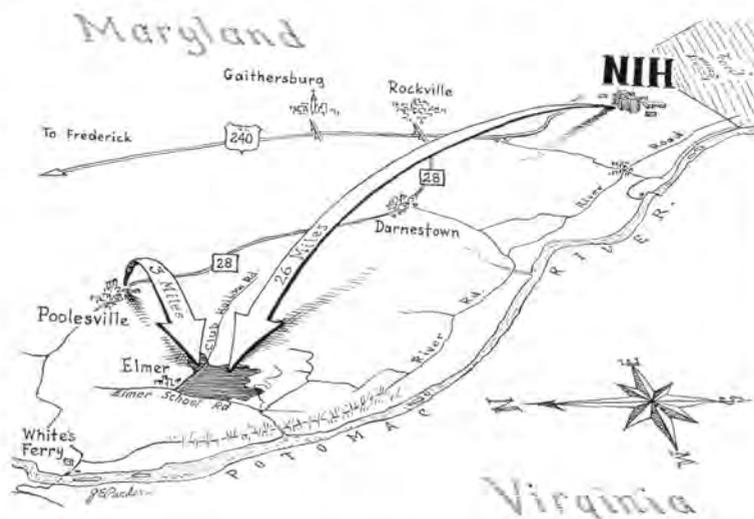
The main areas of investigation at this Center will concern studies in neurophysiology and cardiovascular disease.

The grants in support of these two projects were made by the National Heart Institute from funds especially appropriated by the Congress to the National Institutes of Health for the establishment of primate research centers.

Both Centers will be used by visiting scientists and residents. Each will seek to meet regional as well as national needs.



Dr. Sarnoff



The new NIH Animal Farm is slated to become one of the largest in the country devoted to the production, holding, and treatment of laboratory animals for medical research. This map shows its location in relation to NIH and roads leading from Bethesda. Poolesville is the nearest town, and Darnestown and Rockville are not far distant.

Md., Rm. 317, Ext. 3354. Multiple copies may be ordered from the U.S. Government Printing Office at 10 cents per copy.

## NIAID Grantees Study In Vitro Screening of Therapeutic Enzymes

Prior *in vitro* screening which would facilitate the selection of potentially therapeutic enzymes to treat pulmonary complications in cystic fibrosis is being investigated at Children's Hospital, Philadelphia. Drs. W. S. Chernick, G. J. Barbero and H. J. Eichel have reported this study, supported by a National Institute of Allergy and Infectious Diseases grant, in *Pediatrics*.

The present study demonstrates that pancreatic dornase (deoxyribonuclease) markedly reduced the viscosity of secretions of cystic fibrosis, an effect anticipated to some extent by the investigators because of their earlier finding that tracheobronchial secretions contain a high concentration of DNA. Reduction in the DNA concentration in the secretions and parallel decrease in viscosity of the secretions emphasizes the role of deoxyribonucleoproteins in contributing to the viscid properties of these secretions from cystic fibrosis patients.

### Effectiveness Evaluated

To evaluate the *in vitro* effectiveness of pancreatic dornase and other enzymes on tracheobronchial secretions, specimens were obtained by bronchoscopy in five- to 15-year-old patients with advanced pulmonary involvement.

Spectrophotometric analysis was done on the products obtained by incubation of the specimens with selected enzymes. This revealed that pancreatic dornase rapidly decreased the viscosity of the homogenate and also effected a considerable release of compounds having a maximum absorption at 270 millimicrons.

Of nine other enzymes tested, only two (trypsin and chymotrypsin) caused appreciable hydrolysis of the secretions as reflected by absorption at 270 millimicrons, but these were only a third to a half as effective as dornase in reducing viscosity.

### Serve as Guide

The investigators stress that the procedures they describe should serve only as a guide in the selection of potentially therapeutic agents because factors in the clinical situation are more complex than those of *in vitro* screening. Until controlled clinical studies can be analyzed, caution is advised in using dornase in routine treatment due to the many inherent dangers associated with its promiscuous use.

## County Students Win Summer Fellowships

By John M. Blamphin  
NIH Information Trainee

Seven teenagers in Montgomery County, Md., believe they are among the most fortunate science students in the world.

After attending, with more than 100 others, a series of four weekly lectures in Wilson Hall and a Saturday morning examination on the heart and circulatory system, they emerged as winners of Medical Research Fellowships worth \$200 each.

The fellowships were awarded by the Montgomery County Heart and Tuberculosis Association. The winners will work in National Heart Institute and Naval Medical Center laboratories this summer.

### Locally Sponsored

The fellowships program is sponsored by the County Heart and Tuberculosis Association in cooperation with the National Heart Institute, the Montgomery County Board of Education, and the Naval Medical Center.

It is designed to attract capable, inquiring young minds to the medical profession by providing opportunities for students to learn about and participate in research programs now in progress.

Beginning February 21 of this year and continuing for five weeks, 193 students met on Saturday mornings in Wilson Hall for formal presentations and discussions on open heart surgery, hypertension, and hypercholesterolemia. By means of closed-circuit television, the students toured Heart Institute laboratories.

Only students enrolled in private, public or parochial schools in Montgomery County and who were 16 years of age by June 1, 1961, were eligible for the course.

NHI investigators who spoke at the seminars were Drs. Daniel Deykin, Louis A. Gillespie, John A. Oates, Joseph W. Gilbert, E. Kent Carney, Frederic C. Bartter, Donald

S. Fredrickson, Robert S. Gordon, Jr., and Miss Catherine S. Delea.

A hard-working Summer Fellowships Committee, composed representatives from the cooperating organizations and Montgomery County high school science teachers, first met over a year ago to plan the five-week seminar program.

The chairman was Dr. Bernard H. Ostrow, who is Chairman of the Research Fellowships Committee of the County Heart and Tuberculosis Association. Representatives from NHI were Dr. Bert Boone and Evelyn Trowbridge.

### Questions Suggested

The essay-objective type examination was made up from suggested questions submitted by the investigators who spoke at the seminars. In addition, each student was asked to write a paragraph on his future career plans.

The seven fellowship winners were Joseph Ford, Landon High School; Angelica de Kornfeld and Carol O'Brien, Ursuline Academy; Lawrence Highman and Peter Hoffman, Walter Johnson High School; and Sandra Deanne Ellis and James Johnston, Montgomery Blair High School.

These gifted students, working in a research atmosphere, will become familiar with problems under investigation and the modern methods and skills being used to solve them.

They will learn first hand what research really is.



Students enrolled in the Medical Research Fellowships Competition register for one of the Saturday morning lectures in Wilson Hall.

## NIH Lab Work Included In AU Summer Course For Science Teachers

Secondary school physical science teachers from all parts of the United States will participate this summer in laboratory assignments at NIH in conjunction with an American University Chemistry-Physics Teacher Institute to be held June 26-August 11.

The study-work institute, established in 1956 through a grant of the National Science Foundation, is designed to give the teacher an opportunity to gain new information, techniques, and experience that will enable him to teach in a more stimulating and effective manner.

### Panel Available

The teacher-students will attend morning lectures and work on supervised laboratory studies at American University. From approximately 10 a.m. to 5 p.m. every Wednesday, Thursday, and Friday from June 28 through August 10, they will work at NIH.

A panel of teachers selected for placement at NIH is available for review in the office of Joseph A. Staton, Deputy Chief of the Clinical Center's Clinical and Professional Education Branch, Bldg. 10, Rm. 2-B-50, Ext. 3381 or 3382.

### Examination Requested

In order that teachers may be notified of their assignments as soon as possible, Mr. Staton urges that scientists who wish to take part in the program examine the applicants' credentials at their earliest convenience.

Other research organizations participating in the program are the National Bureau of Standards, the Harris Research Laboratory, and the U. S. Weather Bureau.



Montgomery County teenagers compare notes before a Wilson Hall lecture on Hypercholesterolemia, one of four they attended in the Medical Research Fellowships Competition.

## Metabolic Disease Treatment Progresses in Past 10 Years

The following address was delivered by Dr. George W. Thorn, Physician-in-Chief, Peter Bent Brigham Hospital, and Hersey Professor of the Theory and Practice of Physic, Harvard Medical School, at the Tenth Anniversary celebration of the National Institute of Arthritis and Metabolic Diseases. The RECORD is publishing it in this and the succeeding issue.

The past ten years have witnessed a tremendous advance in our knowledge of diabetes mellitus and of endocrine disorders in general—and in the application of this knowledge toward improving the health and life expectancy of an appreciable proportion of our national population. Thousands of patients now alive and working owe their present state of good health to medical discoveries of the past decade. Diabetic patients alone number more than one and a half million, and it is estimated that an additional one million of our present population will ultimately develop this disorder. In approximately half of these individuals, the disease will become manifest prior to the age of fifty, and of added significance is the fact that all diabetic patients will require, on the average, at least 20 years of medical and dietary supervision.

### Economically Important

Any improvement which can be effected in the overall health of this group of patients, any reduction which can be made in the incidence of complications leading to unemployment or requiring hospitalization will be of great economic significance as well as of humanitarian importance. One can quickly calculate that a reduction of ten cents per day in the average cost of therapy for this group of patients (\$36 per year) or the elimination of one day of hospitalization per year (\$30) or improvement which would result in one additional day of employment per year (\$15) could amount to more than \$100 million annually.

### Others Aided

In addition to diabetic patients, there are a large number of individuals with disorders of adrenal gland function, thyroid, parathyroid, pituitary and gonadal abnormalities who also have been restored to health by the application of knowledge obtained during this period.

A word regarding the significance of studies of endocrine function—the human mind and body owes much of its efficiency and a great deal of its flexibility to the controlled secretions of the endocrine glands. One recognizes this when one realizes that a busy executive often consumes his entire day's food supply in two or three 10-20 minute periods and that the

calories not needed at that moment must be stored in preparation for their momentary mobilization later in the day or night; that any one of us may in the course of a few hours be exposed to external temperatures varying from  $-30^{\circ}$  to  $+110^{\circ}$  F.; that one may walk to his office in the morning and travel at 700 miles per hour in the afternoon; that one may leave his home at sea level to spend a holiday, fishing or skiing, having attained an altitude of more than 10,000 feet that same evening; that in traveling halfway around the world, the body must readjust all of its cyclical functions from daytime rates of activity to those characteristic of our sleeping hours. What is more pertinent to our present discussion, alterations in endocrine function must be of primary importance in accounting for the spontaneous, wide fluctuations which occur in the clinical manifestations of chronic diseases and the spontaneous cure or arrest which may occur occasionally in patients with rheumatoid arthritis, with diabetes, hypertension, or even cancer.

### Reaction Rates Altered

We know now that the secretions of the endocrine glands are potent chemical mediators which provide one of the most important means by which the rates of reactions within the body—chemical, physical, physiological and psychological—can be altered. These humoral substances do not, according to present concept, initiate new chemical or physiological reactions, but they do provide a wide range over which normal body processes can function.

From these considerations it comes as no surprise that a study of the basic facts concerning insulin metabolism and diabetes will lead quite naturally into fundamental knowledge applicable to problems in the field of cardiovascular and renal disease, blindness and other neuropathies; that a study of adrenal gland activity will in turn lead us into problems relating to hypertension, diabetes, psychological disorders and resistance to infections; that a study of the role of the thyroid hormone will provide important information on energy metabolism, cholesterol synthesis and diseases of the muscular system; the parathyroid

## 600 Participate in NIDR Building Dedication

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he said, "have had an opportunity to note that no other profession of our nation has so predominant a world leadership role as dentistry. Here is one field in which the U. S. is acclaimed by all as pre-eminent.

"This fact, coupled with today's increasing concern for improved relationships with other countries," he said, "implies noblesse oblige on our part to give more and more attention to the support of international dental education, dental research, and dental public health, with our lines of communication and service reaching to nations in all parts of the world."

Brief addresses of welcome were delivered by PHS Surgeon General Luther L. Terry and NIH Director James A. Shannon.

### ADA Role Cited

Sen. Lister Hill of Alabama recognized the role of the American Dental Association and the leadership of the late Sen. James E. Murray in the establishment of the Institute in 1948.

Charles Murray, the Senator's son, occupied a chair on the speakers' platform.

Senator Hill predicted that "The Dental Institute, housed in its own building, will add to the prestige and the dignity of dentistry.

"Our dental research specialists," he said, "will now be able to bring together and to concentrate their resources and their energies, up to now dispersed in makeshift and inadequate facilities. They'll be able to press ahead into vital areas of basic and clinical research."

Speaking to (and of) the dental scientists, Rep. John E. Fogarty

of Rhode Island said, "We can give them greater incentive; we can help them indirectly; we can see that they get the trained manpower they need; we can see that the fruits of their studies are used."

But he pointed out that "Only the men and women who work here, by following the tradition of excellence for which NIH is noted, can assure us that the research done in this building will be productive."

### Significance Noted

Dr. Charles H. Patton, President of the American Dental Association, noted that "The significance of this new NIDR facility lies less in its immediate meaning for dentistry than in its ultimate meaning for the American public."

He called attention to surveys revealing that 50 percent of all 2-year-old children have one or more decayed teeth, the average 16-year-old has seven decayed, missing or filled teeth, and 20 million adults have lost all their natural teeth.

"This shameful situation can be alleviated through studies this research institution will make possible," he said.

A reception was held in the main conference room of the new building following the ceremonies. Most of the 600 visitors toured the fourth, fifth, and basement floors, guided by hostesses from the Institute staff.

Institute Directors' secretaries acted as ushers for the dedication ceremonies.

Music for the occasion was by the U. S. Marine Band.



Pictured from an upper window of the NIDR Building is a small part of the crowd of 600 attending the dedication ceremonies, held between showers. Marquee-topped speakers' platform at right, U.S. Marine band at left.—Photos by Jerry Hecht.

on abnormalities in bone, kidney and gastrointestinal function; the pituitary on growth and pigmentation; and a study of the combined pituitary and gonadal systems will provide information important to the geneticist, the gerontologist

and the oncologist.

There is thus no doubt, as one surveys the past ten years, that investigators in the field of endocrine and metabolic diseases have not only made significant contribu-

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## SOVIET DENTAL MISSION TOURS NIH



Members of the first Soviet dental mission to the United States visited NIH and inspected the new National Institute of Dental Research Building on May 17. They are pictured in front of the building with Dr. Francis A. Arnold, Jr., NIDR Director, and Dr. C. Willard Camalier, Director of the Washington Office of the American Dental Association. From left: Dr. Camalier, Dr. A. I. Doinikov, Moscow Stomatological Institute; Dr. Arnold; Dr. A. I. Pozdnyakova, Kiev Medical Institute; Dr. A. I. Rybakov, Moscow Stomatological Institute; Dr. V. I. Karnitski, Omsk Institute, Siberia; and Dr. V. F. Chekin, Director of Laboratory of Surgery, Moscow. The Russians are touring American dental institutions on an international exchange mission as guests of the State Department and the American Dental Association.

## NHI Research Suggests Action of ADH May Be Mediated by ATP Derivative

National Heart Institute studies suggest that the action of the anti-diuretic hormone (ADH) may be mediated by adenosine 3',5'-phosphate, an ATP derivative that has also been implicated in certain of the effects of ACTH, epinephrine, and other hormones.

Antidiuretic hormone (ADH) aids the kidney in maintaining fluid balance by regulating the renal urine concentrating mechanism. It does so by controlling the reabsorption of water in the latter half of the kidney tubule, which, in the absence of ADH, is relatively impermeable to water. Although the site of action of ADH has been fairly well established, the mechanism by which it affects water permeability has not been defined.

### Action Widespread

Studies by NHI scientists suggest that ADH may stimulate the formation and accumulation of adenosine 3',5'-phosphate from ATP in various tissues, and this substance is suspected of being an important common denominator in many hormonal effects. The release of adrenal hormones by ACTH; the release of glucose from liver by epinephrine; the effects produced on the heart by catecholamines; all appear to be accompanied by the accumulation in these tissues of adenosine 3',5'-phosphate.

Since ADH shares with ACTH the ability to release hydrocortisone from the adrenal glands and

with epinephrine the ability to release glucose from liver, the NHI scientists reasoned that adenosine 3',5'-phosphate might also be involved in the effects of ADH on water permeability.

The scientists used the toad bladder for these studies, since others had shown that ADH increases the water permeability of this organ.

### Bladder Divided

The scientists divided the bladder into two separate sacs, one serving as control for the other. Each was filled with Ringer's solution diluted fivefold and was suspended in a bath of normal Ringer's solution. This created an osmotic gradient favoring the movement of water from sac to bath. The net movement of water was estimated by weighing the sacs in air and observing the weight loss in successive 30-minute periods.

Adenosine 3',5'-phosphate and ADH produced markedly similar effects on bladder permeability; added separately to the bath, each caused a substantial increase in water movement out of the sac and each increased the electrical potential across the bladder. Adenosine 3',5'-phosphate also increased the effectiveness of submaximal doses of ADH.

Theophylline, a drug which blocks the inactivation of adenosine 3',5'-phosphate, alone produced effects similar to those of ADH and also augmented the effects of both adenosine 3',5'-phos-

## Heart Output Studies of Six Patients Prove Controversial Starling's Law

The validity of Starling's Law as an important determinant of heart output in man has been demonstrated in studies reported at the recent meeting of the Federation of American Societies for Experimental Biology by Drs. Eugene Braunwald, C. J. Frahm, and John Ross, Jr., of the National Heart Institute Cardiology Branch.

For many years Starling's Law of the heart has been widely used as a major physiological premise in explaining how heart output is modified in accordance with the varying circulatory demands of the body. The validity of this law in certain experimental animals has been well established; however, its applicability in humans has been a far more controversial matter.

### Concept Confirmed

NHI studies have now provided evidence to confirm a concept previously an article of faith to some, a bone of contention to others: Starling's Law is operative in man and is an important determinant of heart output.

Starling's Law states that heart output can be increased by increasing its filling pressure. This produces greater elongation of the heart muscle fibers. Since muscle fibers contract more forcefully from longer fiber lengths (up to a point), the vigor of heart contraction is enhanced and its output per stroke increased.

### Transfusions Used

The studies were carried out in six subjects apparently free from cardiovascular disease. The means for increasing venous return was a transfusion of 1500 ml. of the subject's own blood, previously obtained by several phlebotomies carried out over 7-10 days.

A ganglionic blocking agent was infused throughout the procedure to reduce the activity of the autonomic nervous system. This was necessary because autonomic stimuli can profoundly affect heart contractility independent of the Starling mechanism and can thus obscure its operation. They can also affect blood pressure and resistance to bloodflow by altering the

phate and ADH.

These findings suggest that ADH affects the permeability of the toad bladder, and perhaps the renal tubule, by stimulating the production and accumulation of adenosine 3',5'-phosphate.

Studies aimed at providing more direct evidence for this hypothesis are being carried out in collaboration with Dr. E. W. Sutherland of Western Reserve University, Cleveland, Ohio.

caliber of blood vessels.

Previous studies had shown that, without autonomic blockade, transfusions set off reflexes from pressure-sensitive receptors that largely negated the effects of those transfusions on venous return and heart filling pressure.

### Output Measured

The NHI scientists measured heart output and pressures in the brachial artery, left ventricle, and esophagus before transfusion; and then at intervals of 10-15 minutes during the 30-50 minute transfusion period. These data, and the measures of ventricular performance calculated from them, showed that the transfusions increased venous return and produced a striking elevation in left ventricular filling pressure. This augmented left ventricular performance: heart output per pumping stroke and per minute increased, as did left ventricular work, power, and rate of ejection of blood.

The transfusions were accompanied by significant increases in heart rate in only two of the six subjects.

These findings indicate that ventricular filling pressure importantly affects ventricular contraction, and that Starling's Law, while subject to amendments, is not likely to be repealed in man.

## NEW DRUG

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dide therapy.

More study will be necessary to determine the true measure of the drug's effectiveness against aspergillosis. In a patient with the disseminated disease, marked clinical improvement occurred. Cultures became negative during treatment, but reverted to positive about two months after therapy.

Two patients with pulmonary aspergillosis were treated. In one of these, cultures reverted to positive seven weeks post-therapy, but in the other they remained negative as a result of treatment.

Patients with coccidioidomycosis failed to respond to the drug. However, earlier studies by Dr. Emmons demonstrate its activity against experimental coccidioidomycosis of mice. In the human drug trials, treatment was ineffective in cryptococcosis and candidiasis.

The new antibiotic, not yet commercially available, has demonstrated its usefulness in the treatment of human histoplasmosis, blastomycosis, sporotrichosis, and aspergillosis. There is some experimental evidence that its therapeutic spectrum is wider than may be inferred from these initial studies in patients.

## Dr. Daft Participates In Swedish Symposium, Is Graduation Speaker

Dr. Floyd S. Daft, Director of NIAMD, is the only American among a group of internationally known nutritionists who has been invited to participate in a symposium on "Intestinal Flora and Nutrition," to be held at Bjuv, Sweden, June 12-13.

In a paper entitled "Intestinal Flora and Synthesis of Folic Acid and Pantothenic Acid," Dr. Daft will delineate NIAMD's use of germfree animals in research in the field of nutrition. He will particularly emphasize the role played by intestinal bacteria in the nutrition of the host.

The symposium, which is the second of its kind, is sponsored by the Board of the Swedish journal "Naringsforskning" (Nutrition Reviews).

### Speaks in Iowa

Prior to his departure for Sweden, Dr. Daft was invited to deliver the commencement address at Simpson College during its centennial celebration and graduation exercises at Indianola, Iowa, on June 4.

His presentation, "Simpson's Frontiers—Past and Present," stressed the role of the small college in the educational process, including the preliminary training of research scientists.

Dr. Daft was graduated from Simpson 40 years ago and received his doctorate at Yale in 1926. He was awarded the honorary Doctor of Science by Simpson College in 1952.

## NCI Study Yields Clue To Cell Differentiation

Drs. Eugene J. Van Scott and Richard P. Reinertson of the National Cancer Institute have reported results of a study indicating that the structure and behavior of human skin epithelial cells are governed by their connective tissue environment.

Skin epithelial cells were obtained from 11 patients at the Clinical Center. Nine were skin cancer patients, one had mild psoriasis, and the other had no skin disorder.

### Cells Transplanted

In the experiments, the epithelial cells with and without their connective tissue were transplanted to new places in their own hosts. Thus, mucous membrane from the inner surface of the lower lip, scalp hair roots, and basal cell tumors were implanted in the back; and skin cells of the back and arm were transplanted to the lower lip.

Only when the connective tissue was included did the transplanted cells survive and retain their original characteristics. Otherwise, they either degenerated or developed structural features that often resembled those of epithelium normally resident at the new site.

Research has already established the fact that cells change their structural and functional characteristics when they become cancerous. These experiments were part of a continuing investigation aimed at explaining why this occurs.

A report of the study was published in the *Journal of Investigative Dermatology*.

## Stimulation of Glucose Oxidation Found New Role of TSH in Thyroid Function

Studies by scientists at the National Institute of Arthritis and Metabolic Diseases on the pituitary gland's thyroid stimulating hormone (TSH) suggest that its primary function in the regulation of the thyroid is the stimulation of glucose oxidation in the gland.

Drs. Ira Pastan and James B. Field of NIAMD's Clinical Endocrinology Branch have shown that small amounts of TSH rapidly stimulate the thyroid's ability to oxidize glucose. This effect was seen within five minutes after the addition of TSH to a medium containing thyroid slices.

The fact that TSH, a product of the pituitary's anterior lobe, was effective in such small amounts and so rapidly stimulated glucose oxidation, suggests that this is its primary action on the thyroid and that previously reported thyroidal effects of TSH, such as in iodine and phospholipid metabolism, are secondary.

TSH stimulation of glucose oxidation was specific or peculiar to the thyroid since TSH had no effect on oxidation of glucose by other organ tissue slices, and none of the other anterior pituitary hormones affected the thyroid. It was also shown that the level of TSH present in human blood (a microscopic amount) was effective in stimulating oxidation.

## Financial Aid for Study Rises in Recent Years

Although college tuition costs have risen sharply during the past few years, there has also been an increase in organizations providing financial aid to students.

In a recent study, the Statistics and Analysis Branch, DRG, found that 86% of NIH's FY 1960 principal investigators aged 30 or younger had obtained some formal support (U.S. Government assistance, university scholarship, etc.) during their predoctoral work. Only 10% of those 60 or older had had formal support.

For other age groups, the proportions obtaining formal educational support were: aged 30-34, 81%; aged 35-39, 69%; aged 40-44, 67%; aged 45-49, 62%; aged 50-54, 54%; aged 55-59, 53%.

## Johns Hopkins Awards D.Sc. to Jane Wilcox

Jane Wilcox, Special Assistant for Nursing Research in the Nursing Department of the Clinical Center and a Nurse Director in the Commissioned Corps of the PHS, has been awarded the degree of Doctor of Science by the School of Hygiene and Public Health, Johns Hopkins University.

Two years of Miss Wilcox's study, 1956-58, were sponsored by the PHS.

Although the thyroid's ability to absorb glucose from the medium (glucose uptake) was also stimulated by TSH, this did not seem to be the primary mechanism of the increased glucose oxidation.

This conclusion was reached since insulin, which is thought to act on or to aid the transport of glucose through cell walls, also stimulated glucose uptake but not the oxidation of glucose to carbon dioxide.

### Concentration Rises

In the NIAMD study it was subsequently shown that the increase in glucose oxidation was due to a rise in the concentration of a vital co-factor of glucose oxidation, triphosphopyridine nucleotide.

Acetylcholine, a substance released from nerves to activate muscles and other nerves, also increased glucose oxidation and uptake by the thyroid. However, TSH did not appear to act through acetylcholine as an intermediary, since atropine—an alkaloid used to relieve muscle spasms—inhibited the increase caused by acetylcholine but not that produced by TSH.

Epinephrine, norepinephrine, and serotonin, substances known to stimulate body organs and to affect the thyroid's metabolism of iodine, also were found to stimulate glucose oxidation.

## Dr. Milmore Retires, Takes California Post

Dr. Benno K. Milmore, Assistant Chief of the Epidemiology Branch, NCI, retired from the Public Health Service May 31 after more than 22 years of active service. He has accepted the position of Chief, Bureau of Chronic Diseases, of the California State De-

partment of Public Health, Berkeley.

Dr. Milmore received his M.D. degree from the University of California School of Medicine in 1939 and a Master of Public Health degree from Johns Hopkins University School of Hygiene in 1942.

His association with the National Cancer Institute began in 1954 when he was appointed an epidemiologist in the Field Investigations and Demonstrations Branch.

He was a Lecturer in Public Health at the University of California in 1954, and is a diplomate of the American Board of Preventive Medicine and Public Health.



Monthly Seminars on Administration, sponsored by the NIH Administrative Training Committee for management interns and key administrative officials, are arranged by A. L. Pelmoter, NIH Training Officer. At a recent seminar, Richard L. Seggel, Executive Officer, NIH, led a discussion on the topic "Administrative Management at NIH." He was assisted by this panel of administrative specialists. Seated, left to right: J. W. Finn, Chief Accountant; Mr. Seggel, and J. B. Davis, Chief, Supply Management Branch. Standing: Charles Miller, Chief, Management Policy Branch, and J. M. Sangster, Chief, Personnel Management Branch.

## Test Evaluation Shows Lack of Nystagmus an Index to Consciousness

A preliminary evaluation of a neurological test for newborn infants indicates that all normal newborns should respond to rotation with involuntary rapid movements of the eyeball known as nystagmus. A total absence of this response appears to be a sign of grave abnormality of the nervous system. Since response to vestibular stimulation by rotation may vary considerably in infants, criteria for interpreting the results of this test have been suggested by investigators participating in the National Institute of Neurological Diseases and Blindness' Collaborative Project.

Drs. Murray E. Pendleton and Richard S. Paine, Harvard Medical School and Children's Hospital Medical Center, Boston, tested the eye movements of a series of normal and abnormal full-term newborn and premature infants. An electrically driven table was used to provide constant rates of rotation and deceleration. Photographic and electrooculographic recordings were employed, as was direct observation.

### Some Deviation Noted

The investigators concluded that rotational nystagmus should be present in all normal full-term and normal larger premature infants, provided the infant is thoroughly awake. However, a number of infants were found to exhibit only simple deviation of the eyes with no active nystagmus. This response could be correlated with the following conditions: sleepiness, prematurity, heavy maternal anesthesia, anoxia or traumatic birth, and marked jaundice.

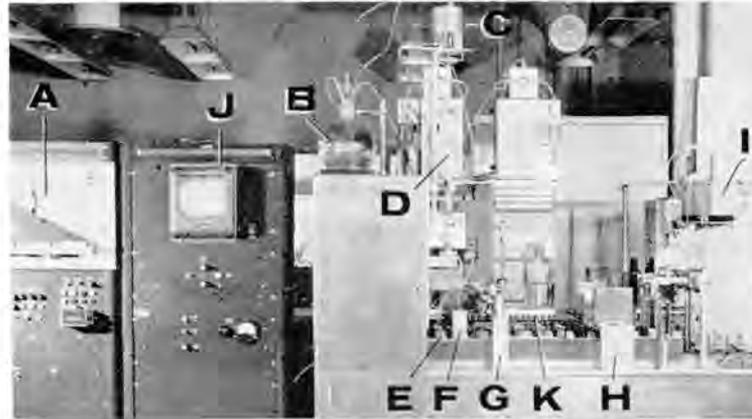
Since an alteration of the state of consciousness is common to all these conditions, the absence of nystagmus appears to be an early and sensitive index to consciousness. In a few infants who exhibited other symptoms of abnormal central nervous system function, neither response could be obtained.

These results confirm that the test for rotational nystagmus is a valuable part of the clinical neurological examination of newborn infants. If abnormal, it is an important clue to depressed nervous system function and an addition to the limited number of criteria available at this age.

### Mary Bouser Leaves NCI

Mary M. Bouser, a Cytology Program Consultant in Nursing in NCI's Diagnostic Research Branch, left NIH May 31 to take a position with the Division of Indian Health, Bureau of Medical Services, in Phoenix, Arizona.

## DRS-Designed Steroid Analyzer Cuts NIAMD Biochemical Research Time



Automatic Steroid Analyzer runs 50 hours unattended.

By George Bragaw

An automatic steroid analyzer, capable of 50-hour unattended runs and containing many unique engineering features, is now in operation in the Laboratory of Chemistry, NIAMD.

The prototype machine automates in two days a complex biochemical analysis that formerly took two chemists a week to complete.

It was designed by Frank O. Anderson, Laurence R. Crisp, Grant C. Riggle, and Gerald G. Vurek, of the Instrument Engineering and Development Branch, DRS.

Biochemical research depends on the availability of accurate and specific methods of analysis. This is especially true of research in the steroid field, where many compounds of similar chemical nature but different biological activity occur side by side in tissues and body fluids.

### Developed in 1954

A new method for the determination of the individual hormones of the adrenal cortex was developed by Drs. Erich Heftmann and David F. Johnson at NIAMD in 1954, based on partition chromatography and gradient elution.

By their method, an extract from urine or tissues, containing a mixture of hormones, is placed on a column of silicic acid, wetted with water. A mixture of petroleum ether and dichloromethane in continuously varying proportions flows through the column and washes down individual steroids in a succession of bands or zones, their movement depending on their relative solubility in the solvent mixture and in water.

The solution leaving the bottom of the column is then collected in fractions of equal volume and can be analyzed separately by physical or chemical methods.

The automatic steroid analyzer completes this laborious process in two days. The machine, pictured above, permits two solvents—in this case petroleum ether and dichloromethane—to be mixed in any

desired proportions by simply plotting the mixing ratio against time on a metal template (A).

The solvents (B) are pumped in the proper ratio into a mixing chamber (C), and then pass into the column (D).

At (E) the effluent from the column is divided into two equal portions by deflecting alternate drops into two sets of test tubes.

### Automatic Processing

After a predetermined number of drops is collected, the column shuts off and the test tubes, moving on a chain-driven rack, are carried on.

As they move at intervals from one station to the next, the solvents are first evaporated at (F), then alcohol is added at (G) and the residue is dissolved by vibrating the tubes.

A third row of test tubes, containing only alcohol, serves as a check on the chemical analysis. Reagents are added to one of the pair of steroid-containing test tubes and also to the control tube at (H).

### UV Absorption Measured

After a 20-minute mixing period, the color in these two tubes is compared in a colorimeter (I). At the same time the ultraviolet absorption in the second steroid fraction is determined in an adjacent spectrophotometer.

The readings of both analyses are recorded on a moving graph (J), and the solutions are stored at (K) for further experiments.

The steroid analyzer was nearly three years in design and construction, and even before it was placed in use it created considerable interest among biochemists in this country and abroad.

It was designed for maximum

## Dr. R. C. Arnold Appointed Chief, PHS Personnel

Dr. R. C. Arnold, Assistant Surgeon General for Personnel and Training and one-time Chief of the Technical Services Branch of the National Heart Institute, has been appointed Chief of the newly created Office of Personnel in the Public Health Service.

Paul M. Camp, who headed the former Division of Personnel, will be Deputy Chief.

Under the reorganization, the Office of Personnel will have a Division of Commissioned Officer Personnel, headed by Dr. Elton S. Osborne, Jr., and a Division of Civil Service Personnel, directed by William H. Carr.

### Cites Advantages

Establishment of the new Office, Surgeon General Terry pointed out, will enable PHS to give increased emphasis to recruitment, career-development, and other personnel activities formerly carried on at the Divisional level.

A member of the PHS Commissioned Corps since 1931, Dr. Arnold held the post of Director of Syphilis Research at the Venereal Disease Research Laboratory at Staten Island before coming to NIH in 1951. He left in 1956 when he was designated Chief of the Heart Disease Control Program in the Bureau of State Services.

### NCI Associate Director Title Change Announced

The title of the Associate Director of Chemotherapy, National Cancer Institute, has been changed to Associate Director for Collaborative Research, according to a recent announcement by Dr. Kenneth M. Endicott, NCI Director.

The change has been made necessary because of the added responsibilities of the Virus and Cancer Program.

In addition to occupying this position, Dr. Stuart M. Sessoms will continue as Chief of the Cancer Chemotherapy National Service Center.

flexibility and safety of operation. With minor modifications, it can be used for the automatic analysis of other types of chemical compounds.

A technical paper and a film showing its operation and engineering features were presented last November at the 13th Annual Conference on Electrical Techniques in Medicine and Biology, in Washington, D. C.

## Hamsters Present Play June 16-17 and 22-24

"The Skin of Our Teeth," a Pulitzer Prize-winning three-act play by Thornton Wilder, comes to NIH next week in a split-weekend, five-performance presentation by the R&W Hamsters.

The play will be given on June 16, 17, and 22, 23, and 24. All will be evening performances at 8:30 in the CC auditorium.

### Special Showing Planned

The opening night's performance (June 16) is for CC patients, their families and friends, without charge. The remaining performances are open to NIH staff and the public. Tickets are \$1.25 each.

Alice and Frank Barnhardt have the leading roles as Mr. and Mrs. George Antrobus of Excelsior, New Jersey, a pair of average Americans at grips with destiny, fire, flood, pestilence, the seven-year locusts, the ice age, the black pox, the double feature, and the late-late show.

### Cast Numbers 32

Walter Clark and Greta Albrecht play the Antrobus' two children, Henry (Cain) and Gladys. Carmen Cabrera plays the fortune teller and Jeanine Fair plays Sabina. There are 32 parts in the show.

The play is directed by Paul Blank, assisted by Jack Robinson. Ozzie Grabiner is business manager.

Tickets are available at the CC Film Desk and through representatives in each building. For further information call Betsy Slay, Ext. 4161.

## 15 Institutions Awarded PHS Fellowship Grants

The Public Health Service has announced the award of seven five-year Senior Fellowship grants and 10 Special Fellowship grants to investigators in 15 universities and schools of medicine and dentistry in 12 States.

Cost of the awards, for the first year will be \$154,214 for Senior Fellowship grants and \$149,991 for Special Fellowship grants.

These awards, made under the program administered by the Division of General Medical Sciences, were approved by Surgeon General Terry on the basis of recommendations by the National Advisory Health Council at its March 1961 meetings.

The Senior Fellowship grants are awarded to institutions in the United States in behalf of individual investigators, and are intended to encourage and support the development of professional personnel for academic and research careers in medicine, dentistry, public health, and related areas.

## Service, Ideas, Performance Win Cash For Three Staff Members of DRS

Three members of the Division of Research Services received awards totaling more than \$500 at a ceremony held recently in the office of Chris A. Hansen, DRS Chief. These cash awards represent the three types available to employees who make outstanding contributions in the form of service, ideas, or work performance.

The award winners were Elmer Horman, a supervisor of animal caretakers in the Laboratory Aids Branch, and Donald Heckard and Stanley Paul Allen, both employees of the Plant Engineering Branch.

Mr. Horman's award was for special service in the scheduling of incoming monkeys through the quarantine procedures and tuberculin testing each receives in the Animal Hospital.

Mr. Horman was recognized for his effective handling of a highly complicated work schedule that involves the daily care of nearly 1,000 monkeys and the immediate processing of new shipments without disruption of the care and feed-

ing routines for the entire colony.

Mr. Heckard is an equipment inspector in the Planning and Control Section. His suggestion that push-button switches be purchased to replace key switches formerly installed in the watchman tour system in the Clinical Center has since been adopted as a saving in both maintenance and replacement costs and as a convenience to the guard force. It will save NIH an estimated \$2,210 over a 10-year period.

Mr. Allen, a mechanical engineering technician of the Engineering Design Section, responded to an unprecedented workload owing to a shortage of engineers by performing mechanical engineering work at a much higher level than his normal duties.

He has saved NIH an estimated \$15,000 in engineering fees by assuming full responsibility for technical calculations and decisions involved in major mechanical installations and renovations totaling some \$300,000.



Three DRS staff members are pictured with DRS Chief Chris A. Hansen, following presentation of performance awards at a ceremony in his office. From left: Elmer Horman, Laboratory Aids Branch; Mr. Hansen, and Donald Heckard and Stanley Paul Allen, both of the Plant Engineering Branch.

## METABOLIC

(Continued from Page 4)

tions within their primary areas of interest but have, in addition, provided ideas, techniques, and personnel for research in the more difficult fields of degenerative diseases, cancer, and mental illness.

How has it been possible to bring about such important advances so rapidly? In part this is related to the solid background of training and experience in the basic sciences achieved by many of the investigators in this field. Secondly, techniques for clinical investigation carried out by this group

have included precise chemical and physiological measurements, and this group of scientists in particular have appreciated the need for adequate, experimental control. At a relatively early date, this group of investigators also sought the skills of the mathematical sciences for conceptual schemes as well as for statistical and analytical methodology.

### Effort Is Unified

Finally, there was achieved in this area, again at a relatively early period, an important unity of effort among scientists within educational institutions, the pharmaceutical industry, and federal

## Harold Halpert, NIMH, Named to New Post In Community Services

Harold P. Halpert, Chief of the Publications and Reports Section, NIMH, has been appointed to a newly created position in that Institute's Community Services Branch.

In his new assignment Mr. Halpert will provide consultive services to State and local mental health agencies. He will work closely with DHEW Regional Offices in helping to develop and strengthen mental health programs through application of improved communication techniques and procedures.



Mr. Halpert

### Worked With Navy

Before coming to NIH in 1952, Mr. Halpert was associated with the Bureau of Personnel, Department of the Navy, as an Education Specialist. He has also held positions with the Department of the Army, the Office of Education, and the Federal Security Agency.

A native of New York City, Mr. Halpert was graduated magna cum laude from New York University in 1932, with honors in English. He received his M.A. degree from the University of Illinois in 1933 and did graduate work at Columbia University. From 1943 to 1948 he was a part-time instructor in English at George Washington University.

Mr. Halpert's new office is located in Room 301 in the Robin Building. His extension is 8447.

agencies such as the National Institutes of Health. The farsightedness of the latter is to be commended in making available research fellowships and training grants which have increased so effectively the use of grants allocated by its several Institutes for research purposes.

It is not possible at this time to detail the wide scale program of research which the National Institute of Arthritis and Metabolic Diseases has fostered in the field of diabetes and endocrine diseases. We can note that the policy of the Institute has been particularly effective in facilitating the early application of fundamental discoveries made by scientists all over the world as well as of those within its own laboratories. Also its programs of long-range basic science investigation have provided a continuing source of stimulation for its active program of applied clinical investigation.

(To Be Continued)