

the

FILE COPY.
Record

U. S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE

Vol. XII, No. 7
March 29, 1960

PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

Drs. Dorn, Shapiro And Alt Heading New Branches

A Biometrics Research Branch has been created in the National Heart Institute, under the direction of Dr. Harold F. Dorn, former Chief of the Biometrics Branch, DRS. The latter Branch has been dissolved.

The transfer of Dr. Dorn and his staff to NHI will expand the application of biometrics to cardiovascular research.

Also established this month, in the Division of Research Services, were the Computation and Data Processing Branch and the Instrument Engineering and Development Branch.

Developed from the Statistical Processing Section of the defunct DRS Biometrics Branch and from the Instrument Section of the Laboratory Aids Branch, the two new branches in DRS reflect the increased NIH needs for data processing and instrumentation services.

Dr. Norman Z. Shapiro will direct the new branches.
(See *NEW BRANCHES*, Page 8)

Library Assistance Available at Night

A library assistant, Fred D. McLeod, has been assigned to night duty at the circulation desk of the NIH Library, which remains open until 10 p.m., Mondays through Fridays.

NIH staff members wishing to use the library during the evening hours may obtain needed assistance from Mr. McLeod.

April Panel Discussion Sponsored by NIMH

The fifth in a series of special meetings for NIH information officers, to be held here April 14, will be sponsored by the NIMH Information Office.

Panel members will be Harry Milt, Public Relations Director for the National Association for Mental Health, New York City; Robert L. Robinson, Director of Public Relations for the American Psychiatric Association, Washington, D. C.; and Harold P. Halpert, Chief, Publications and Reports Section, NIMH.

Programs of Breadth and Stability Stressed at NIH Budget Hearings

By Ken Stabler

Testifying on the NIH 1961 budget estimate before the Subcommittee of the House Committee on Appropriations, Dr. Shannon observed that NIH programs are "directed to general rather than specific progress in research, to institutional stability, and to development of resources to permit

full use of the investigators' talents."

The NIH Director attributed the strengths of current NIH research processes to "the increasing maturation of programs that at their inception were sound in principle."

These programs, he said, "have now become established and essential parts of the Nation's medical research effort."

Other Administrators Testify

Other NIH administrators who appeared before the Committee, headed by Rep. John E. Fogarty, included the seven Institute Directors and the Director of the Division of General Medical Sciences.

Each was questioned at length and presented a statement and documents relating to his portion of the budget, including his area's Highlights of Research Progress and Program Development, setting forth major accomplishments of 1959.

Cites Research Support

"Today," Dr. Shannon said, "our programs support more than one-third of all medical research in this country. Thousands of young men and women are being aided while they complete their postgraduate training for research, academic, and service careers. And hundreds of research laboratories are being constructed or renovated, in part with matching grants from our appropriations."

Dr. Shannon said he believed that "these established and accepted activities in support of the individual"—which, he noted, represent more than 85 percent of NIH's 1960 activities—"should con-

(See *BUDGET HEARINGS*, Page 7)

PROGRAMS PLANNED FOR LIBRARY WEEK

The third annual National Library Week, April 3 to 9, will be observed at NIH with exhibits of reading aids, story hours for children, a panel discussion, and an open house in the Patients' Library.

The week's events are directed toward stimulating the interests of CC patients and NIH personnel in the pleasures and rewards of reading.

One of the highlights of the program will be a panel discussion at 7:30 p.m., April 6, in the CC 14th floor assembly hall, on favorite books and authors.

Panel members are Dr. Morris Belkin, Head, Cellular Pharmacology Section, NCI; John E. Fletcher, Chief, ORI; Lealon E. Martin, Deputy Chief, ORI; Roy Perry, Chief, Photographic Section, DRS; Hazel Rea, Administrative Officer,

(See *LIBRARY WEEK*, Page 2)



A patient who cannot raise her head can read with the benefit of prism glasses. Here, Judith Le Grand, of the CC Patients' Library, demonstrates the glasses which bend on image 90°.

Health Campaign Lag Scored by Committee; Participation Urged

The PHS mid-March report on the current Federal Service Campaign for National Health Agencies and Joint Crusade showed NIH lagging with only 18 percent participation. BSS reported 51 percent and BMS 37 percent participation.

The campaign ends April 15.

In announcing the first two weeks' results the NIH Campaign Committee pointed out that for several years PHS has lagged behind non-health agencies in percentage of participation, despite the fact that the prime aim of the campaign is to provide support for health agencies.

The Committee also reminded NIH employees that they number about 7,000 of the PHS total of approximately 9,900, and urged each NIH keyman to make sure that all employees in his group are aware of these worthy causes and have been encouraged to participate.

The Committee noted two encouraging items: Dewey Shurtleff, keyman for Biometrics Research Section, NHI, reported 100 percent and DGMS 77 percent participation.

COSTEP Files Open

Files of students eligible for employment under COSTEP are available for review and selection in Rm. 2B-46, Bldg. 10. All persons interested in making a selection are urged to do so as soon as possible.

the Record

Published bi-weekly at Bethesda, Md., by the Public Information Branch, 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.

Editor.....E. K. Stabler

Associate Editor.....Elizabeth D. Mok

Staff Correspondents

Elaine Johnson, NCI; Robert Hinkel, NHI; Kathryn Mains, NIAID; Lillie Bailey, NIAMD; John Kley, NIDR; Lucille Furman, NIMH; Pat MacPherson, NINDB; Elsie Fahrenthold, CC; Mary Henley, DBS; Janet Gallagher, DGMS; Phyllis Snyder, DRG; Virginia Lundblad, DRS.

NEWS from PERSONNEL

Commissioned Officer Personnel Bill

The Commissioned Officer Personnel bill is in Congress now awaiting final action. The bill is intended to strengthen the Commissioned Corps of the Public Health Service through revision and extension of some of the provisions relating to retirement, appointment, and other related personnel matters.

The bill was passed by the House on March 9. However, because of last minute additions making certain effective date changes, it must go back to the Senate for passage by that body again. In view of the earlier favorable action by the Senate, it is anticipated that the bill will be passed in substantially its present form.

Blood Donations

On Tuesday, April 12, the American Red Cross Bloodmobile will again be receiving blood donations from NIH employees. The unit will be set up at Wilson Hall between the hours of 9 a.m. to 1 p.m. Volunteers must be over 18 and under 60 years of age. Donors under age 21 must have written permission from a parent or guardian. Appointment blanks are available in the Employee Relations and Services Section, Bldg. 1, Rm. 21.

Classification Standards

In recent months, the Civil Service Commission has revised the position classification standards for Clerk-Typist, Clerk-Stenographer, and related clerical positions. The purpose of these new standards is to combine 17 previously existing series (related groups of positions) into about five new series of work.

This change does not affect present grades. Should an employee receive a notice of change in his position title and have questions about it, he should contact the Personnel Assistant in his area.

Superior Performances Win Awards for Two

Superior performance awards were presented to two NIH employees in March.

Ruby H. Peters, Supervisor, Appropriation Accounting Unit, Accounting and Auditing Section, OAM, received a check for \$350 on March 9 for devising a new and simplified system for the payment of research grants.

The new system has resulted in a substantial savings in the disbursement of funds through a greatly reduced number of check issuances.

On March 15, Preston H. Grantham, a chemist in the Nutrition and Carcinogenesis Section, Laboratory of Biochemistry, NCI, received a check for \$175 for developing a rapid micro-method for the determination of ionization constants of organic chemicals, making it possible to accelerate investigations in his Institute.



Recent awards presentations were made in individual ceremonies. At left, Ruby Peters, OAM, receives her award from G. A. Van Staden, Chief, Financial Management Branch. Preston H. Grantham, NCI, (left), holds his check and receives congratulations from Dr. Harold P. Morris, (center), Chairman of the Awards Board, and Dr. John R. Heller, Director, NCI.

Review of Grants Requests Is a Complex Procedure

By Betty Mok

The thrice-yearly NIH Advisory Council meetings, just concluded for the spring session, have reviewed a portion of the 13,904 research grant applications submitted for this fiscal year—the highest number received in any 12-month period. The March sessions complete the allocations of about \$200,000,000 in grants funds for FY 1960.

Dr. Weinbach, NIAID, To Study Abroad

Dr. Eugene C. Weinbach, NIAID, Laboratory of Parasitic Diseases, will spend a year abroad, beginning April 1. Most of this time will be spent at the Wenner-Grens Institut, Stockholm, where he will study problems of mitochondrial biochemistry. Dr. Weinbach plans also to visit laboratories in England and Holland before he returns to NIH in the spring of 1961.

LIBRARY WEEK

(Continued from Page 1)

Clinical Investigations, NIMH; and Mrs. William C. Jenkins, wife of Dr. Jenkins, NIMH.

At its open house on Friday, April 8, the Patients' Library, Rm. 5N-262, Bldg. 10, will display talking books, electric page turners, prismatic reading glasses, ceiling projectors, and other reading aids available to patients who have difficulty with vision or with holding a book or turning pages.

National Library Week is sponsored by the National Book Committee, Inc., in cooperation with the American Library Association. The NIH program has been arranged by Margaret C. Hannigan, Patients' Librarian.

The administration of these funds, which total just under 50 percent of the 1960 NIH budget, involves approximately 700 NIH personnel, from clerks to top administrators, and some 600 leading non-government special consultants serving as members of study sections and advisory councils.

A look behind the mass of statistics which represents the NIH research grants program reveals a well-planned and efficient mechanism for analyzing, recording, reviewing, rating, and awarding research grants to scientists throughout the world. Using a hypothetical applicant, the procedure works like this:

How It Works

Dr. Joseph Augustus Doakes, a professor and research scientist in a mid-Western university, plans to conduct a study of amino acid metabolism and needs funds to support it. He submits a grant application, bearing the formal approval of his university, to NIH. The application consists of a detailed description of the project and what he hopes to accomplish, as well as a complete budget setting forth his estimate of costs.

Dr. Doakes' application reaches the DRG mail room in a flood of a thousand or so others just before the deadline date for the winter Study Section meetings. His application is logged in by the DRG project review officer, a scientist-administrator familiar with all the disciplines, who determines to which study section Dr. Doakes' application will be sent for review, and which Institute will subsequently be responsible for presenting it to one of the eight Advisory Councils.

Sections in Four Groups

The Study Sections, now numbering 35, are organized into four main groups: clinical research, biochemical and biophysical sciences, biological sciences, and health services. These categories contain the whole range of modern medical and biological scientific investigation.

The 10 to 15 non-government members of each Study Section, appointed for a 4-year term, are authorities in their particular fields of medical and biological sciences. During the two to four days they meet (three times each

(See GRANTS REQUESTS, Page 8)



Science Section

This four-page section, devoted chiefly to summaries of research findings that have been reported by scientists of the National Institutes of Health, is prepared with the cooperation of the Information Offices of the Institutes and Divisions of the National Institutes of Health.

Collaborative Studies Seek Brain Damage Source

An understanding of when and how brain damage takes place is essential in the effort to achieve the eventual prevention of cerebral palsy, mental retardation and related disorders of infancy and childhood. The source of the damage is now believed to lie in the period surrounding birth—from conception through labor and delivery and until about one month after birth.

It is estimated that there are approximately four and a half million mentally retarded persons in this country. About one-third of these are children and the disorder afflicts about 126,000 children each year. In addition, some 550,000 persons are afflicted with cerebral palsy, two to five percent of our school children are reported to have speech disorders, four percent have hearing impairment, and 35,000 school children are legally blind.

In an attempt to find the answers to these large national problems, a collaborative research program related to cerebral palsy, mental retardation and other defects in children was officially begun January 1959, after two and a half years of intensive preparation.

This is the first large-scale effort to collect information on all factors which might conceivably relate to these neurological disorders and the first research program ever undertaken to collect and analyze this information before rather than after such disorders develop. The National Institute of Neurological Diseases and Blindness is serving as coordinator and central laboratory for the project.

Central Services Expanded

The central services for the collaborative perinatal project have been expanding and will continue to expand during 1960. There have been two major objectives: first, to forge a strong and closely knit organization of the collaborators and the central office; and second, to refine the data collection procedure.

To build a well knit organization, small working subcommittees have been established in special areas of the study. These have included obstetrical, pediatric, and neurological examinations; psychological testing; and interviewing.

The members of the subcommittee have worked closely at Bethesda with the central staff, and in some instances, have served as staff members for the development of certain facets of the project. This association has not only increased the actual participation of the collaborators in the central planning, but has aided in coordinating the total program.

In addition to the active working sessions, thirty-five meetings involving principal investigators in various areas of the study have been held this year. Plans have been reviewed, protocols established, and policy decisions made regarding the scientific development of the project.

Protocols Tested

Recognizing the importance to the study of accurate and complete reporting, the reliability and validity of protocols have been further developed and tested during the past year. A carefully refined protocol for listing accurate and detailed family health and socioeconomic data has been worked out. A series of obstetrical examinations has been critically reviewed, and the obstetrical subcommittee has established procedures to achieve accurate recording of these essential data. A detailed protocol for the examination of the

(See PERINATAL, Page 5)

Concept Challenged On Enamel Protein

While previously published analyses of enamel protein have shown wide variability, they have at the same time agreed in reporting the presence of large amounts of glycine, proline, and hydroxyproline. Largely from such data it might be concluded that enamel protein belongs to the collagen class. This concept has now been challenged by a National Institute of Dental Research chemist reporting at the International Association for Dental Research meeting on recent studies of the protein matrix of human enamel.

Analyses Performed

Recognizing the possibility that previous samples may have been contaminated with varying amounts of dentine collagen, Dr. Karl A. Piez, Laboratory of Biochemistry, performed a series of complete amino acid analyses of enamel proteins carefully isolated from unerupted third molars. Through the use of special apparatus designed to give precise analysis, it was found that the protein was nearly all soluble in the decalcifying solution. Moreover, the soluble protein contained no hydroxyproline or hydroxylysine and only moderate amounts of glycine indicating that it was not a collagen. While its composition showed several distinctive characteristics, it was unlike any other known protein. The small insoluble residue was similar in composition to the soluble protein if the presence of about one-third collagen is assumed.

Thus it is suggested that results from previous amino acid analyses were influenced by contamination with dentine collagen as well as losses of enamel protein owing to its solubility.

Manifestation of Polyoma Virus Studied by NIAID

The ability of the mouse polyoma virus to produce multiple tumors in mice and other rodents has aroused great interest and stimulated extensive studies of virus by many laboratories. One of the basic questions raised in relation to this virus is, "What manifestations does the polyoma virus produce as it occurs naturally?"

Drs. Wallace P. Rowe, Robert J. Huebner, and Janet W. Hartley of the National Institute of Allergy and Infectious Diseases reported recently on studies of the natural occurrence of polyoma virus in mice (*Mus musculus*) inhabiting densely populated areas of New York City, particularly Harlem.

The NIH scientists were aided in the field work by the New York City Health and Sanitation Department. Approximately 1,000 mice were studied. The natural history, the importance of ecto-parasites, the mode of spread of the virus, and the tumorigenic activity of "wild" polyoma virus strains were studied. The basic tool for these studies is the hemagglutination-inhibition test, which serves both as the indicator of past infection and the end-point of sensitive virus detection tests in laboratory animals and tissue culture systems.

Frequency Varies

In the Harlem area infection was found in high frequency along certain blocks, while nearby blocks were completely negative. There was marked difference in frequency of infection of mice trapped in different apartment houses within a single block. Virus was recovered from the organs of 14 wild mice, and also twice from floor sweepings in apartments housing infected mice. Virus was isolated from the excreta of three of the mice. Mites recovered from infected mice were found negative for the virus. Cockroaches trapped in the apartments were also negative.

Excretion of virus apparently plays an important role in its transmission in nature. In laboratory experiments, infected newborn mice have been found intense sources of environmental contamination. Eating and drinking contaminated food and water appeared to be possible modes of entrance of virus into mice. However, inhalation of virus appears to be a more effective mode of entry.

The important question of the

(See POLYOMA, Page 4)



This baby is having an otological examination at John Hopkins Medical Center, one of the 17 institutions participating in the collaborative project.

Tumors Associated With EEG Patterns In NINDB Studies

An electroencephalographic (brain wave) pattern, which recurrently occurs in patients with idiopathic petit mal epilepsy, has also been found, with statistically significant frequency, in patients with brain tumors. Detailed findings of two cases where tumors were associated with this EEG pattern and an extensive review of similar cases indicate that the abnormality which produces the typical "petit mal" pattern may lie within the brain stem. Unlike many other types of epilepsy, seizures which show this pattern usually cannot be correlated with gross or microscopic lesions in the brain.

Among the most striking and typical in clinical EEG, these brain wave recordings are characterized by bilateral, symmetrical 3/second wave-and-spike complexes. Studies relating this pattern with pathological findings were recently reported by Dr. C. Ajmone-Marsan and Dr. W. R. Lewis, National Institute of Neurological Diseases and Blindness Electroencephalography Branch, at the Eastern EEG Association Meeting, Ste. Marguerite, Quebec, Canada.

In the two cases examined by the investigators, both EEGs showed the typical pattern, highly suggestive of petit mal epilepsy. In the first subject, a large metastasis of one cerebellar hemisphere was found, but the patient had no history of epileptic seizures. In a second case, the patient demonstrated petit mal, as well as temporal lobe epilepsy and generalized convulsion. Here, a large astrocytoma extending into the thalamus was removed from the right temporal lobe.

Because cases of brain tumors associated with bilateral 3/second wave-and-spike patterns are so rare, statistical evaluation was devised to assure that a valid relation existed between the two phenomena. The respective incidence of brain tumors and of the "petit mal" pattern were calculated for the general population. Results showed that if chance alone were operating, an association of the two factors would occur in 48.2 out of a million cases. However, data from three published reports totaling 1,071 brain tumors resulted in an "actual" frequency of 6 cases, as compared to an "expected" occurrence of .0517 case on the basis of chance. According to the investigators, this discrepancy is significant enough to warrant the conclusion that the phe-

Metabolic Role of Glucagon Suggested by NHI Studies

Glucagon, the pancreatic hormone which liberates stored sugar from the liver, has been found by National Heart Institute workers to also liberate fatty acids from storage in fatty tissue. The scientists have been especially interested in the finding that glucagon, and various other hormones that effect the release of stored energy, have a similar enzymatic effect in body tissues, suggesting the possible existence of a common mechanism involved in lipid mobilization.

It is becoming increasingly clear that the release of fatty acids, a major metabolic fuel, from the adipose tissue depots is subject to a variety of hormonal controls. It has been shown previously by Dr. Robert S. Gordon of the National Heart Institute that epinephrine stimulates release of fatty acids from fat depots. Adrenocorticotrophic hormone (ACTH) of the pituitary has also been shown by several investigators to stimulate release of fatty acids. Recent studies by NHI investigators have added another hormone glucagon, to the growing list and revealed an interesting mechanism that may help to clarify the way in which hormones exert their stimulating action on fat mobilization.

Dr. Martha Vaughn, Dr. Daniel Steinberg, and Dr. Eleazar Shafir in the Section on Metabolism of the National Heart Institute have demonstrated a stimulating action of

Figures Reported on Mental Health Studies

The National Institute of Mental Health, in cooperation with the State Mental Health Authorities, established a program of statistical reporting in 1954 for outpatient psychiatric clinics. The first report based on material for 1955-56 indicates that an estimated 379,000 persons were clinic patients during the year. About 197,000 children and 182,000 adults made up this patient load. The estimated number of patients per 100,000 population was higher for children than adults, and higher for males than females.

phenomena are related.

The predominant extra-cortical, mid-line location of brain tumors in the cases examined as well as in all similar cases reported in the literature suggests that the brain stem plays a significant role in the production of this very characteristic, yet still mysterious, EEG pattern.

the pancreatic hormone, glucagon, on release of fatty acids both in the living animal and *in vitro*. The effect in the whole animal had been overlooked in previous work because the initial response to glucagon injection is a fall in blood fatty acid levels. This fall coincides with the period during which the blood sugar is elevated due to the action of glucagon on the liver. By following the fatty acid levels over a period of 24 hours the NIH workers observed a late rise in fatty acid levels beginning only after blood glucose levels returned to normal.

Phosphorylase Level Raised

Both epinephrine and glucagon were known, from the work of Dr. E. W. Sutherland and colleagues at Western Reserve University, to increase the levels of the enzyme phosphorylase in the liver and thus lead to more rapid release of glucose from the liver. This suggested examination of the adipose tissue to determine whether the mechanism of action in that tissue might be related to the demonstrated mechanism of action in the liver. It has now been shown that these two hormones do indeed raise the levels of active phosphorylase in the adipose tissue. The pituitary hormone, ACTH, had been shown by Dr. Robert Haynes to do in the adrenal cortex what epinephrine and glucagon do in the liver, namely, increase the amount of the enzyme phosphorylase. The present work shows that ACTH also increases the amount of phosphorylase in the adipose tissue. The connection between the effects of these hormones on phosphorylase and their effects on release of fatty acids remains to be determined.

It is intriguing to find that these three hormones, each of which has well-defined metabolic effects in the liver or in the adrenal cortex, are all active in the adipose tissue. The adrenal cortex responds to adrenocorticotrophic hormone but apparently not to epinephrine and glucagon. The liver responds to epinephrine and glucagon but not to adrenocorticotrophic hormone. Adipose tissue responds to all three. This is of interest with respect to the general problem of tissue differentiation. A common final path is suggested for the mechanism by which the hormones act and further studies may clarify the biochemical nature of the hormonal control.

The NIH investigators published their findings in the *Journal of Clinical Investigation*.

Procedures Revised On Sterility Tests

Amendments have been adopted to revise sterility test procedures for biological products. The revision of one of the basic tests is designed to ensure the purity of all licensed biological products and reflects recent advances in manufacturing procedures as well as in scientific achievement.

As of April 15, 1960, manufacturers of biological products subject to control under the Public Health Service Act will be required to follow the revised procedures for sterility testing. Redesignated as Section 73.73 of the Public Health Service Regulations, these requirements are designed to ensure the freedom from extraneous microorganisms of all licensed biological products. The revision represents a composite scientific opinion based on years of research and, in the judgment of those experienced in the practical aspects of production, is essential to the rapid progress made in this field in recent years.

The timeliness of the adoption of United States sterility test standards is emphasized by the recent recommendations of the World Health Organization. The participation of Dr. Margaret Pittman, Division of Biologics Standards, in the WHO Study Group which formulated these recommendations at the Geneva Conference a year ago, facilitated the efforts of DBS in drafting comparable requirements. Although the U.S. standards are more detailed and specific, they are consistent with those recommended by WHO. This is expected to be of considerable help not only to U.S. producers of biologics engaged in foreign commerce but also to foreign manufacturers who export biologics to this country, since the latter must also be licensed to comply with U.S. standards.

POLYOMA

(Continued from Page 3)

relation of polyoma virus to the occurrence of spontaneous mouse neoplasms was also discussed at the Gustav Stern Symposium by Dr. Rowe. He described studies undertaken with the collaboration of the Roscoe B. Jackson Laboratories, Bar Harbor, Maine, where large numbers of mice of various inbred strains and hybrid combinations are observed for life and autopsied when moribund from any cause. Polyoma antibody in tumorous mice was compared with that in mice dying without tumors. Among the inbred strains there was not the slightest indication of any excess of polyoma antibody among tumorous mice compared with comparable non-tumorous mice. In the hybrids the situation was essentially the same.

PERINATAL

(Continued from Page 3)

placenta has been developed, and a manual for placental examination is now available. The manual is accompanied by kodachrome slides depicting the characteristic changes to be reported.

Procedures Changed

A protocol for the neurological examination of the newborn infant has been developed and has been subjected to a test-retest analysis. On the basis of these findings, important changes in the procedure have been recommended. A training film demonstrating the technique of the examination of the newborn has now been completed. Also, a rigorous pretest of the development examination for the eight-month old infant has resulted in various procedural changes.

A procedure has been established for the collection of blood specimens from the pregnant woman for virus studies. A coldroom is now equipped at NIH and blood specimens from patients studied this year are being carefully filed for future virus studies. Under contract, antigens of some 40 known viruses are being prepared. More than three-quarters of these are now available and it is anticipated that within the next six months, antigens for all these agents will be on hand. The team of scientists responsible for conducting the serological studies is now in training.

Statistical Base Broadened

In addition to the 5500 mothers and 4200 babies studied in the pretest phase of the project, 3300 mothers and 1800 babies had been studied in 1959 in the final study series as of October 1. The project also envisages the study of other groups of women and their offspring not delivered in the collaborating institutions. This will aid in determining the representativeness of the pregnancy experience in the collaborating institutions and will broaden the statistical base of the project by bringing into it additional numbers of damaged cases.

Methodologies Developed

In December 1958, arrangements were made with the Columbia University School of Public Health and Administrative Medicine to explore the needs and methods of this "extensive phase" of the collaborative project. In January, a conference of some twenty outstanding investigators was held to outline the needs and methods of this phase of the study. Since then, a small working committee has been formed which is concerned with the further development of these methodologies. To

CANCER STUDIES CONTROL DIET



Rigorously controlled studies of the metabolism of cancer patients are being carried out by the Metabolism Service of the National Cancer Institute's General Medicine Branch. These pictures illustrate one approach to obtaining information on clinical manifestations of malignant disease. Top left: This fat extraction apparatus is used to determine the amount of dietary fat consumed and the amount excreted by cancer patients. Top right: As part of the "balance study techniques", food is prepared and measured to meet the individual needs of cancer patients. The composition of the diet is calculated by the dietitian, and all the food and fluid are weighed and/or measured to insure that the patient gets exactly the same amount of food each day. Food for the entire study is obtained from the same source to insure a constant intake. During each study, samples of the complete day's diet are sent to the laboratory for analysis. Bottom: A metabolic kitchen where food is carefully prepared and measured to meet the individual needs of cancer patients.

date, two ongoing pretests have evolved.

The Columbia University group is now studying the methodology for case finding in the New York area. Their objective is to determine methods of detecting cases of cerebral palsy, mental retardation, blindness, deafness and other neurological disabilities, and relating the findings in these patients to the prior recorded events of pregnancy and labor. This study will also aid in collecting accrued figures of prevalence and incidence, and in evaluating the sample being

collected at the New York Medical College and Columbia University School of Medicine.

Larger Sample Taken

In another study, with the Kaiser Foundation and the University of California at Berkeley, women receiving prepaid medical care are participating in a study similar to the collaborative project but with less detailed observation. This will make possible a larger sample, approximately 8,000 women a year.

As a result of these activities,

Cultures' Resistance To Light Damage Effected by Dye

During studies of poliovirus by plaque assay technique, Division of Biologics Standards virologists observed that the top layer of monkey kidney culture would frequently degenerate within 48 hours after application of overlay medium. Since this raised a problem in interpretation of viral assays, a study was undertaken to determine the cause of this degeneration.

Experiments were conducted to determine the variables of temperature, dye, and light. The results indicated that the combination of neutral red dye and light was the damaging factor. However, when cells stained with neutral red were incubated in the dark overnight, cell degeneration did not occur following exposure to light. Although other workers have described the occurrence of photodynamic action on cells, development of resistance to photodynamic action has not been reported previously.

Eliminates Cell Degeneration

From a practical point of view, the discovery makes possible the elimination of unexpected cell degeneration during virus assay by shielding the infected cell cultures from light during the initial 12-16 hours of the 6-day incubation period.

Of academic interest is the mechanism by which cell resistance developed. There were two possibilities: the resistance could be due to a change in the cells, or to alteration of the dye. Cultures which had developed resistance to light after incubation with neutral red for 48 hours were also found to be resistant to sensitizing action of the addition of fresh dye. This indicated that loss of sensitization was probably due to a change in the cells rather than alteration of the absorbed neutral red. Furthermore, when neutral red was extracted from resistant cell cultures and applied to fresh cells, the cell cultures died after exposure to light, indicating that there was no alteration in the dye.

A complete report of this work, co-authored by Alice M. Gochenour and Samuel Baron, Division of Biologics Standards, was published in a recent issue of the *Proceedings of the Society for Experimental Biology and Medicine*.

and under the surveillance of the planning committee, a well-rounded total program is evolving. Its objective is to evaluate those factors in pregnant women which influence the health of their children and interfere with the achievement of their full potentiality.

Cataract Studies Show Enzyme Side Effects

Alpha chymotrypsin, an enzyme which facilitates cataract surgery by fragmentation of the fibrils in the suspensory ligament of the lens (zonula fibers), is found to injure the endothelial lining of rabbit corneas, although the damage is usually temporary. This injury does not seem to be of a specific nature. Related studies show, for the first time, that endothelial cells multiply by mitosis, or indirect division.

The report of a National Institute of Neurological Diseases and Blindness committee investigating the use of alpha chymotrypsin was presented by Dr. Ludwig von Sallmann, Chief, Ophthalmology Branch, NINDB, at the annual meeting of the American Academy of Ophthalmology and Otolaryngology. The report summarized the findings of a cooperative study suggested by the Academy to investigate the effects of the enzyme on other parts of the eye.

In studies by Dr. von Sallmann, alpha chymotrypsin was infused into the anterior chamber of the eye of young rabbits, and removed after three minutes with washings of 0.9 percent saline solution. Subsequent examinations showed that the corneal endothelium was frequently injured. In some of the experiments, varying degrees of corneal clouding were found to occur. In these instances, large defects of the endothelium could be detected microscopically. Damage confined to a small area usually disappeared after 24 hours, although extensive corneal clouding sometimes persisted for more than five weeks. Control animals infused solely with 0.9 sodium chloride also occasionally exhibited endothelial damage.

Because of the difficulty of examining the endothelium, a new technique was devised in which the entire cell population of this tissue could be studied. Flat mounts of the whole endothelium were prepared by dissecting layers of the excised corneas under a stereomicroscope. A significant result of this technique was the demonstration that cells in the endothelium of adult animals multiply by mitosis, contrary to previous assumptions that division was amitotic, or by direct cleavage. In animals with extensive injuries, cell regeneration by mitotic activity was greatly increased.

Results of preliminary tests of the allergic effects of alpha chymotrypsin, conducted by Dr. G. van Alphen of the Ophthalmology Branch, NINDB, were included in the report. Here, guinea pigs were sensitized by repeated injections of the enzyme. Challenge doses a month after sensitization did not produce noticeable allergic

NIAID Studies Indicate Environment No Factor in Parasite Transmittal

The high incidence of intestinal parasitism in patients in mental institutions has been attributed variously to crowded conditions and to inherent untidiness among these patients. A unique study designed to determine the possible relationship between housing facilities and parasitism in mental patients reveals that transmission of intestinal protozoa continued despite greatly improved housing and sanitation of the group during the three years of the study.

Dr. Geoffrey M. Jeffery of the National Institute of Allergy and Infectious Diseases Laboratory of Parasite Chemotherapy field station in Columbia, S.C., reports his findings in the *American Journal of Hygiene*. Prior to removal to modern quarters from an extremely outmoded building, a core group of 110 white female patients ranging in age from 18 to 76 years were examined for intestinal parasites. Nine series of examinations were conducted, 4 during the first year (1954), 3 the second, and 2 the third year. This group was studied for the entire 3-year period and were examined on all 9 occasions. In addition, 199 patients had 1 to 8 examinations, depending on the length of time they remained at the South Carolina State Hospital, site of the study.

The physical environment of the patients was also checked regularly, including gross inspection for fecal contamination of the buildings and exercise yards, plus surface sampling of floors, walls, and furnishings by the use of cellulose tape. Twenty-six sites within the building were sampled for examination each time.

The incidence of 7 protozoan species from infected inmates was tabulated. Of these species (*E. histolytica*, *E. coli*, *I. butschlii*, *E. nana*, *C. mesnili*, *T. hominis*, and *G. lamblia*) only *C. mesnili* and *T. hominis* showed a net decrease in incidence between initial and final examinations. Some helminths (hookworm, *Strongyloides*, *Trichuris*) were also surveyed, and a small reduction in the percentage of patients infected was observed; of these, *Strongyloides stercoralis* showed the most pronounced reduction.

A single striking increase in in-

responses. These studies may indicate that adverse reactions to alpha chymotrypsin are unlikely to occur in patients previously treated with the enzyme for other disorders, or where it is used a second time for a cataract operation.

cidence was observed in the protozoan *E. nana*. With this organism, an initial 19.1 percent incidence rose to 62.7 percent on final examination.

Dr. Jeffery believes his data justify the assumption that transmission of protozoa continued steadily throughout the study. The rate of acquisition of protozoa appeared to lessen, however, during the last year or more of residence in the new quarters. The helminths present a different picture. After the patients were transferred to a modern building there was no evidence of hookworm transmission, and only 3 cases of *T. trichiura* occurred which could be attributed to residence in the building.

The question of persistence of parasitic protozoa, according to Dr. Jeffery, is clouded by the distinct possibility that prolonged occurrence of a given parasite in an individual might represent a number of infections of short duration rather than prolonged infection. In extrapolating probable percentages of infections within periods of 5, 10 and 20 years, based on average percent of infection per year, in general the parasite species which apparently persist for the longest periods are those with the highest prevalence at any one time. The persistence of hookworm and *T. trichiura* infections for the full three-year period in almost all cases is indicative of the normally long persistence of these parasites in untreated populations. In work subsequent to that described in this report, it has been shown in this same group that these parasites continue to persist in the majority of cases for at least 5 years.

Skin Collagen Changes May Relate to Age

Dr. William G. Banfield, National Cancer Institute's Laboratory of Pathology, has reported that the amount of acetic acid-soluble collagen present in human abdominal skin varies in an orderly fashion throughout life.

The results of the present study show that until age 20 soluble collagen gradually decreases, from age 20 to 40 it decreases more sharply, and then rises again. At 60 to 80 years of age, 80 percent of individuals whose skin was tested showed soluble collagen. After age 80, soluble collagen declines slightly.

The paper was published in a recent issue of the *AMA Archives of Pathology*.

Methotrexate Studies Confirm Prior Findings

Dr. Abraham Goldin and Stewart R. Humphreys in the National Cancer Institute's Laboratory of Chemical Pharmacology have reported further results in their continuing studies of the effectiveness of dihalogenated derivatives of methotrexate in prolonging the life of mice with transplanted leukemia L1210. (*Journal of NCI*)

The current study of immunity in mice surviving the systemic disease confirms preliminary findings that many of the long-term survivors are markedly immune to reinoculation of leukemic cells, the new inoculum showing no or very slow growth. Other data suggest that the leukemia must be sufficiently far advanced, possibly systemic, for eradication of the disease by treatment with the drugs to be accompanied by the development of immunity.

The authors conclude that the drugs act, at least in part, by influencing the host-tumor relationship so that the mice become immune. Thus, the importance of understanding the interrelationships of the host, tumor, and drug in the chemotherapy of cancer is again emphasized.

Grafted Pituitaries Function Partially

Dr. Roy Hertz, Chief of the National Cancer Institute's Endocrinology Branch, has reported detailed studies on the growth pattern in young rats which were hypophysectomized (pituitary gland removed). Then multiple pituitary grafts were implanted underneath the kidney capsule in the same rats from which pituitary was removed. The grafts supported substantial somatic growth—about two-thirds the normal rate—but failed to maintain normal thyroid, adrenal, and gonadal function.

These results contribute to clarification of the relationship between hypothalamus and pituitary, and show that in the rat, production and secretion of growth hormone are not completely dependent upon an intact hypothalamic-pituitary system. Furthermore, the data suggest that such pituitary grafts, which are known to increase the incidence of breast cancer in mice, may be exerting their tumor-enhancing effect at least in part by producing growth hormone. Moreover, these data indicate that the demonstrated beneficial effects of pituitary stalk section in breast cancer patients may not be mediated through suppression of growth hormone.

The paper appears in a recent issue of *Endocrinology*.

Dr. Stetten Speaks At Brooklyn College

Dr. DeWitt Stetten, Jr., Associate Director in Charge of Research, NIAMD, delivered the Murray B. Gordon Lecture on March 7 at the Downstate Medical Center, State University of New York in Brooklyn.

Selected for the honor in recognition of his outstanding contributions to medical research, Dr. Stetten lectured on "The Role of Glycogen in Health and Disease."

Dr. Stetten has recently returned from a trip to Dallas, Texas, where he attended the annual meeting of the Dallas Diabetes Association and discussed the results of his trip to Russia.

BUDGET HEARINGS

(Continued from Page 1)

continue to be the central focus of our programs."

He observed, however, that these activities "pose no major problems of either a policy or an operating nature." He told the Committee that "the primary task . . . of developing effective means for Federal funds to share in the support of individual research projects and postgraduate training, while at the same time assuring the freedom and integrity of the grantees and their institutions, is behind us."

Grantee Needs Unsatisfied

Viewing the other aspect of the picture—the weaknesses in the approach to research support, which he said had become increasingly apparent during the present fiscal year—the NIH Director pointed out that, ". . . There is abundant evidence today that . . . the needs of the grantee institutions are not being met. The universities, medical schools, and other centers for research and teaching in the health sciences serve the people in three ways: in research, in education, and in public service. Their institutional needs are overwhelming, and the means for satisfaction of those needs are inadequate."

Cites Possibilities

In discussing this problem Dr. Shannon stated:

"The point may be made that if the Nation's system of educational and research institutions were financially capable of doing so, they could with their own resources or with resources wholly controllable by them:

"1. Provide a stable background for current activities supported by outside funds.

"2. Extend research to include opportunities newly apparent to the medical investigator . . .

"3. Provide an organizational structure for the grouping of diverse disciplines and approaches

WHO Cancer Officer Visits NIH on U.S. Tour

Dr. Helen E. Pogosianz, Chief Officer, Cancer Section, World Health Organization, Geneva, arrived at NIH March 14, beginning a month's visit in this country to consult with leading cancer investigators and research directors.

Prior to her two-year appointment to WHO in June 1959, Dr. Pogosianz had served since 1945 as Laboratory Chief, Institute of Experimental and Clinical Oncology, Academy of Medical Science, Moscow.

Arrangements were made by the Cancer Institute for Dr. Pogosianz to visit staff members of cancer research institutions in Baltimore, Philadelphia, New York, Boston, Bar Harbor, Buffalo, Chicago, San Francisco, and Palo Alto.

While in New York she will attend the Symposium on Phenomena of Tumor Viruses, and in Chicago, the meeting of the American Association for Cancer Research.



Dr. Helen Pogosianz

New Post for Dr. Syme

Dr. S. Leonard Syme, who joined DRG on January 4, has been appointed Executive Secretary of the Division's Public Health Research Study Section.

Prior to his recent appointment, Dr. Syme assisted Glenn G. Lamson in administration of the PHR Study Section and the Hospital Facilities Research Study Section.

Mr. Lamson continues as Executive Secretary of the latter Section.

centered about broad disease categories, without at the same time distorting the fundamental structure and function of the institutions of higher learning.

Reporting on the present approach to solution of this problem, Dr. Shannon said:

" . . . In presenting our programs to the Congress, we will present proposals for improving the mechanisms, and the terms and conditions, through which support for research is provided. The ways in which funds are made available affect the productivity of investigators, and are therefore as important as the dollar level of support and the kind of research which is aided.

"For an activity such as ours, with focus on support of the research component of non-Federal institutions, there is an obligation to provide such support under terms and conditions which recognize and seek to ameliorate the institutions' dilemma, or at the very least do not increase their already pressing problems.

"There are a number of ways in which the 1960 NIH program and the 1961 proposal reflect our con-

Dr. Berry to Attend WHO Symposium

Dr. Elmer G. Berry, NIAID Laboratory of Parasitic Diseases, will attend the WHO Symposium on Bilharziasis March 30 through April 8 in Lourenco Marques, Mozambique. At the request of WHO, Dr. Berry has prepared a working document, "Snail Control by Chemical Means," for consideration at the meeting.

cern over institutional strength and stability."

Chairman Fogarty then interjected.

Mr. Fogarty: Do you have any tangible evidence of this trend?

Dr. Shannon: You have reference to the larger grants particularly?

Mr. Fogarty: Yes.

Dr. Shannon: Yes, sir. It was increasingly apparent by 1956 that as our programs extended in scope, our ability to develop a long-range program with high productivity would in no small measure be determined by our ability to modify our granting procedure so as to give seasoned investigators greater freedom of action and greater assurance of continuity of support.

Following a series of questions and answers relating to the amount of an average grant and increased costs in the grant program, Dr. Shannon said:

"The research projects grants, without deviation from standards of excellence, continue to follow a trend toward larger grants for more broadly defined objectives, with support committed for longer periods of time. This trend is the product of the changing nature of

Mongolism Research Outlined in Pamphlet Prepared by NINDB

NINDB scientists are currently engaged in a broad program of basic research to find the causes and prevention of mental retardation.

One phase of the research effort is described in the pamphlet, "Mongolism—Hope Through Research," prepared by NINDB and published this month as PHS Publication No. 720 and Health Information Series No. 94.

Mongolism, so-called because its victims tend toward Oriental facial characteristics, is a severe form of congenital mental retardation which afflicts more than 35,000 infants born in the U.S. every year.

Mentality Limited

The typical Mongoloid seldom achieves a mental capacity beyond that of the three- to seven-year old child and rarely lives a normal life span. Mongolism occurs in all races and in children born to parents from all walks of life.

A great many theories have been advanced as to the cause of this condition. One, widely held, has been that early in pregnancy some unknown factor interferes with the normal development of the embryo.

New Theory Reported

A more recent theory, reported in the pamphlet, is that the disorder may be caused by an irregularity in the ovum before it is fertilized. British and French investigators have reported that in nine Mongoloids studied, each had 47 chromosomes instead of the normal 46. Chromosomes are the microscopic life threads in each cell which determine inherited characteristics.

The discovery of this extra chromosome may be a significant advance in the search for the cause of Mongolism. It may also hold a clue to the mystery of why Mongoloids are born more often to older than to young mothers.

scientific endeavor and the significant increase in the funds available, but it has positive value to the stability of the institutions where the research is carried out."

At one point in the hearings Chairman Fogarty expressed an interest in awards received by NIH personnel. Dr. Shannon subsequently supplied him with a list (contained in the published report of the DHEW hearings) of the 14 NIH scientists who received major awards and honors from non-Federal organizations during 1959, with a description of the award received by each.

Dr. Willey, DGMS, To Resign in April

Dr. Richard R. Willey, Chief of the Research Grants Branch, DGMS, will leave his post early in April. He expects to devote the ensuing eight to 10 months to travel and study prior to making future plans. His successor has not yet been named.

Dr. Willey has been at NIH since 1954, when he was appointed Executive Secretary of the Mental Health Study Section, then a unit of NIMH and later made a Study Section of DRG. He became the first Grants Branch Chief of DGMS when the Division was organized in 1958.

Born in Cincinnati, Ohio, Dr. Willey received his Ph.B., B.S., and Ph.D. degrees in psychology, from the University of Chicago. Since 1951 he has held the positions of research associate in psychiatry and psychology and department advisor to the Department of Psychology at the University of Chicago; research associate with the Council of State Governments; executive assistant of the American Psychological Association; and consultant to the Southern Regional Education Board. He served in the U.S. Army Air Corps from 1943 to 1946.

A party will be held in his honor at Top Cottage, April 1, at 4 p.m. All of Dr. Willey's NIH friends are invited.

GRANTS REQUESTS

(Continued from Page 2)

year, several weeks prior to council meetings), it is their job to review the applications and select those which seem most likely to make significant research contributions. Members reach a collective judgment on each application, and on those which they feel are worthy of NIH support, they assign a priority number.

The priority ratings, along with a summary of the various opinions of each application, are submitted by the Study Section executive secretary (a scientist appointed to the DRG staff) to the proper Institutes for further staff work and presentation to the appropriate advisory councils.

Each of the seven Institutes and the Division of General Medical Sciences has its own Council, composed of distinguished leaders in science and public affairs, who study, discuss, approve, or reject each application. Their final opinions occasionally differ from those of the Study Sections. Their recommendations are passed on to the Surgeon General. The members have the additional responsibility of considering policy and over-all

ANALYZER IS PRECISE, TIME-SAVING



An automatic amino acid analyzer is operated by Dr. Karl A. Piez of NIDR. This instrument, based on principles developed at the Rockefeller Institute, was designed in its present form by Dr. Piez and was built in the Instrument Section, Lab Aids Branch, DRS. It employs a gradient device ("Varigrad"), seen as the cylindrical assembly of plastic tubes at left-center, designed by Drs. Elbert A. Peterson and Herbert A. Sober of NCI. The analyzer not only saves a great deal of manual labor but provides a high degree of precision in performing amino acid analyses. It operates by means of chromatographic separation and chromatographic analysis of the separated components. For a description of the analyzer's use in enamel studies, see page 3.

program objectives of the Institute concerned.

Dr. Doakes' application has now been approved by both the Study Section and the Advisory Council, and he is duly notified. He knows that he is free to conduct his research as he sees fit, to publish his findings at any time, and that he may apply for a further grant if his studies are not completed at the termination of this one.

The Doakes grant is only a tiny portion of a program that has been expanding steadily each year since its inception in 1946. In that year, the first in which money was appropriated to NIH for the purpose, there were between 100 and 150 grant applications and a total grants appropriation of \$780,000.

By 1956 the applications had risen to 4,636 and the appropriation to \$38,000,000. In the next five years the applications increased 200 percent more, and appropriations reached the \$200 million mark.

Over the years the program has become a major force in strengthening medical research and stimulating new studies in previously neglected fields.

NEW BRANCHES

(Continued from Page 1)

rect the Computation and Data Processing Branch, with headquarters in Rm. 728, Bldg. 12. Benjamin H. Baker will be Administrative Officer.

The Branch will have responsibility for the centralized operation of automatic data processing machines and equipment at NIH.

The group will also conduct studies designed to make maximum use of data processing equipment in meeting the research needs of NIH.

The Instrument Engineering and Development Branch, located in Rm. 3512, Bldg. 13, will be under the direction of Dr. Fred Alt, with Marion Carr as Administrative Assistant. In addition to the design and fabrication of specialized equipment, and the maintenance and repair of instruments, the Branch will provide consultation in laboratory instrumentation to Institute scientists and investigators.

Transferring to NHI with Dr. Dorn are Jacob Lieberman, Beulah

Berlin Scientists Here For Dental Research On Enamel Structure

Prof. Johann-Gerhard Helmcke and Miss Liselotte Schulz have arrived here from Berlin under the Visiting Program for nine months' work on dental enamel structure in the NIDR Laboratory of Histology and Pathology.

Well known in Europe as a biologist and outstanding electron microscopist, Prof. Helmcke is Chief of the Research Group in Micromorphology at the Fritz-Haber Institute of the Max Planck Society and is also professor of biology and anthropology at Berlin Technical University.

The Micromorphology Laboratory has been active both in research and training, and has published extensively in the field of electron microscopy. Miss Schulz is an electron microscopist who has assisted Prof. Helmcke since 1954.

Prof. Helmcke is a member of many biological societies and is editor of the *Handbuch der Zoologie*. He worked closely with the pioneers who were instrumental in the early development and exploitation of the electron microscope, later devoting his efforts to the study of tooth and bone structures. He has placed special emphasis on stereoscopic electron microscopy, and micro-electron diffraction.

Sunrise Service At Walter Reed

The annual Easter Sunrise Service at Walter Reed Army Medical Center, which the public is invited to attend, will be held at 6:30 a.m., April 17, in the Center's formal gardens.

The U.S. Army Band and the 40-voice choir of the First Presbyterian Church, Arlington, Va., will participate in the service.

Guest speaker will be Dr. Frederick W. Helfer, pastor of the Christian Temple, Baltimore, Md.

Dulaney, Doyn Scruggs, Betty Mills, and Lorraine McDonald. Added to the staff are Dewey Shurtleff, Dean Krueger, Dorsey Offutt, Audrey Hairston, and Margaret King, all members of the old NHI Biometrics Section.

Dr. Dorn, who has specialized in biometrics at NIH for the past 13 years, will continue to head the survey relating smoking habits to health in 290,000 veterans.

This study received national headlines several years ago when it established a relationship between heavy smoking and lung cancer. Similar statistical links are being explored between smoking and other diseases.