

PHS Grants Aid New Centers for Clinical Research

Eight special research grants totaling \$2,974,408 to assist in the establishment of clinical research centers, were announced recently by Acting Surgeon General John D. Porterfield of the Public Health Service. The program is being administered by DGMS.

The awards, first of their kind, will provide a new type of resource permitting intensive controlled study of a limited number of patients as part of the clinical research activity of the institutions receiving the grants.

Directed by Congress

The grants were awarded on the basis of recommendations to the Surgeon General by the National Advisory Health Council. The action was taken within guidelines set by the Congress in reports related to the 1960 Labor-HEW appropriations bill, in which NIH was directed to initiate a new program of grants for "therapeutic and metabolic research units."

In those guidelines, the need for additional resources to facilitate the more complex type of clinical investigations in a broad spectrum of diseases was emphasized, and the bill provided additive funds in

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Registration Begins June 1 For Employee Health Plans

NIH employees will begin registering for the much discussed and long-awaited Federal Employee Health Benefits Program on Wednesday, June 1. The registration will continue through June 24.

Those eligible to enroll in the program will be furnished registration forms (SF-2809) and instructions by the designated Registration Assistants in their areas.

NIH Library Becomes Branch Under Clopine

The Surgeon General, PHS, has approved an organizational move elevating the NIH Library from a section in the Scientific Reports Branch to branch status in the Division of Research Services. The change was effective April 20.

John J. Clopine, NIH Librarian since June 1959, regards the move as a significant step forward in the library's long history of service to science.

"Dr. Milton J. Rosenau established the Hygienic Laboratory Library in 1901," he said. "Let's imagine that it began with the medical classics of the day and random copies of bacteriological journals."

"The NIH Library has come a long way since. One milestone was the merger of the Public Health Service Library with the NIH Library in 1942.

"We attribute the library's new status to internal recognition of

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Each eligible employee (see eligibility listing, Page 8) will also receive a kit containing information essential to selection of the plan best suited to his individual needs.

Eligibles Must Register

The Personnel Management Branch points out that all employees who are eligible for enrollment are required to register even though they may not elect to enroll in one of the four insurance plans.

The information kits, now being distributed, contain the following: 1) a memorandum outlining the program, 2) suggestions for the assistance of employees in selecting a plan, 3) a list of Registration Assistants with their room numbers and telephone extensions, and 4) brochures explaining the Government-wide Service Benefit Plan, the Government-wide Indemnity

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Key Job Changes Involve Dr. Mider And Dr. Smadel

Dr. Joseph E. Smadel, NIH Associate Director for Intramural Research, has been named Chief of the Laboratory of Virology and Rickettsiology, DBS, by Dr. Shannon. His appointment becomes effective July 1.

He will be succeeded by Dr. G. Burroughs Mider, now Associate Director in Charge of Research, NCI. Dr. Mider's new position will be designated Director of Laboratories and Clinics.

Commenting on Dr. Smadel's



Dr. Smadel

Dr. Mider

new appointment, Dr. Shannon said:

"Dr. Smadel has desired for some time to return to the laboratory and continue his research career, and I have reluctantly acceded to his request. He has served with distinction since joining my staff in 1956. I know, however, that science generally, and particularly the fields in which he has won international recognition, will gain as a result of Dr. Smadel's return to the bench."

Continues as Chairman

Dr. Smadel will continue to serve as chairman of the joint United States-South East Asia Treaty Organization cholera research project.

In his position as Director of Laboratories and Clinics, Dr. Mider will be Dr. Shannon's principal policy assistant and advisor on all intramural programs, including certain research operations in field installations not previously receiving policy and program review by

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NIH DRUG DISCOVERY IS SHARED ABROAD

Secretary of State Christian A. Herter in an "Instruction" sent recently to U. S. diplomatic posts throughout the world announced that this country is making available to all other countries detailed information concerning the manner in which the new analgesic drug, phenazocine, may be synthesized.

Secretary Herter pointed out that the new drug, discovered by Drs. Everette L. May and Nathan B. Eddy of NIAMD, is a more powerful painkiller than morphine, yet safer to use.

"The impact abroad of our mak-

ing this discovery available," said Mr. Herter, "should be of considerable value in furthering our foreign policy objectives. Every opportunity should be utilized to present and obtain favorable publicity for our Government's humanitarian action and purpose in dedicating its significant discovery to the peoples of the world."

Reprints of the definitive papers dealing with the chemical nature and synthesis of phenazocine, published in the *Journal of Organic Chemistry* (Oct. 1959) by Drs. May and Eddy, were sent with the State Department document.

Save With 'Surplus'!

Through the cooperation of the Surplus Property Utilization Program, the Division of Research Services recently obtained a \$17,000 bulldozer and a \$14,000 road grader without cost, the Supply Management Branch reports.

SMB points out that thousands of items are handled through this program monthly and suggests: "Why not try this source of Supply?"

The NIH excess property display area is located in Bldg. 12, Rm. G110. For information, call Ext. 4215.

the Record

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Scientific Developments Reported at Meeting Of Information Staffs

A presentation of reports on the programs and scientific developments of NIH Institutes and Divisions featured the May 5 staff meeting of NIH information officers. The program, arranged by NINDB, marked the sixth in a series of special monthly meetings.

The reports, presented by the information officers or members of their staffs, will be published in the Science Section of the *Record* beginning with this issue. (See Page 3.)

Speakers, Topics Listed

The participants and their topics were: James F. Kieley, NCI, "Environmental Cancer"; Hugh Jackson, NIAMD, "A Replacement for Morphine"; Robert R. Hurt, NIDR, "Dental Epidemiology Goes Abroad"; Daniel Bailey, DGMS, "What's New in Aging"; Francis J. Olson, CC, "Normal Volunteers"; Arlene Butterly, DBS, "Research in Biologics Control"; Donald R. Goldthorpe, NIAID, "Respiratory Virus Research"; Alexander Adler, DRG, "Changes in the Research Grant Picture"; William E. Sanders, NHI, "Cardiovascular Drug Development"; and Dale B. Kloak, NIMH, "Dreams." Chairman for the meeting was Ruth Dudley, NINDB.

LIBRARY

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the many services it performs daily for the scientific community at NIH. The excellence of its present collection of 85,000 medical volumes is a direct result of the foresight of earlier librarians. The journal collections in chemistry, biochemistry, biology, and medicine are exceptionally strong."

Another recent development in the library's history is the crea-

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the amount of \$3 million for this purpose.

Dr. Porterfield pointed out that the financing of these clinical research centers under PHS grants is focused on resources that will permit more effective development of broad programs of clinical research, and not on the support of individual research projects.

The grants initially will pay for renovation and equipping of facilities, and subsequently the total support of these units, including bed costs, immediate supporting laboratories, and the salaries of the specially trained professional staff and ancillary personnel required by such a facility.

Grantees Named

Research projects which may be made possible through the use of these specialized research resources will continue to be eligible for support separately under the research project grant system.

Institutions receiving the grants are: University of Southern California School of Medicine, Los Angeles; Emory University School of Medicine, Atlanta, Ga.; Johns Hopkins University, Baltimore, Md.; University of Michigan Medical School, Ann Arbor; Washington University School of Medicine, St. Louis, Mo.; Bellevue Medical Center, New York University, New York City; University of Pennsylvania School of Medicine, Philadelphia; and University of Washington School of Medicine, Seattle.

tion of the position of Assistant Librarian. Anna E. Dougherty, formerly with the National Library of Medicine, was appointed to the new post in December 1959.

Policy guidance for the NIH Library is provided by an advisory committee of scientists representing NIH Institutes and Divisions. Dr. Heinz Specht, Chief, Laboratory of Physical Biology, NIAMD, is chairman.

NIH GETS ANIMAL FARM PROPERTY



Friday, May 6, was a historic day for NIH. At 11 a.m., in the Washington office of the Lawyers Title Insurance Corporation of Richmond, Va., Isadore Brill and Harold E. and Rhoda Luber, co-owners of the old Cider and Ginger Farm near Poolesville, Md., met with Chris A. Hansen, Chief, DRS, and James A. King, DRS Executive Officer, to deed the farm over to NIH. It will be used as the site for an animal farm. The sale price was \$145,000. In this picture, Mr. Brill (right) receives a check for that sum from Matthew M. Epstein, the Justice Department attorney who guided the title acquisition transaction. At far left is Manuel B. Hiller, the DHEW attorney who represented PHS interests. Mr. Hansen (second from left) headed the site selection committee that searched from July to November 1959 for acreage convenient to NIH. Mr. King (second from right) did much of the behind-the-scenes work required for the transaction.

KEY CHANGES

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the Associate Director for Intramural Research.

Dr. Smadel received his B.A. degree from the University of Pennsylvania in 1928, and his M.D. degree in 1931 from Washington University, St. Louis. Before joining NIH in 1956, he was Director of the Division of Communicable Diseases at the Walter Reed Army Institute of Research.

Dr. Mider, a recent winner of the DHEW Distinguished Service Award, was graduated from the Cornell University Medical School in 1933. He was appointed a research fellow of the National Cancer Institute in 1938 and later became a member of its research staff.

He has also served on the faculties of the Medical College of Cornell University, the Medical School of the University of Virginia, and the School of Medicine and Dentistry of the University of Rochester.

Western Reserve Gets Aging Research Grant

The Division of General Medical Sciences has made a grant of \$186,000 to Western Reserve University, Cleveland, Ohio, to support a broad program of research in aging, PHS Surgeon General Burney announced recently.

Arthur S. Flemming, DHEW Secretary, delivered an address at Western Reserve on May 11 in connection with the grant.

This is the third grant by the Public Health Service since 1957 to support large, comprehensive, research programs on aging within university settings.

The programs permit scientists of different fields of interest to integrate their studies on the problems of aging. The two earlier grants were to Duke University and the Albert Einstein College of Medicine.

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.

Volunteer Normal Controls Are Young and Dedicated

By Francis J. Olson

Chief, Information Service, Clinical Center

Webster defines a volunteer as one who enters into, or offers himself for, any service of his own free will. The words "free will" are very important when used in connection with the Volunteer Normal Control Program of the Clinical Center.

Healthy volunteers as normal controls in medical research is not a new concept. They have been used by physicians from the first dawn of medical history. To understand what is abnormal, one must first know what is normal.

Our Clinical Center volunteers are a unique group—young men and women, mostly of college age, who cheerfully enlist in the cause of medical research by becoming long-term patients. They come from widely scattered sections of the country, from farms and small towns and, occasionally, from big cities. Some are students looking for more education. Others are looking for new experiences or new friends.

Public Service Pledged

But they have two things in common: most of the volunteers come to the Clinical Center through either the Brethren or Mennonite churches, and they are dedicated to their volunteer work because it is part of the public service they have pledged to God. Most are members of one of these churches, but members of several other faiths have volunteered. And there have been groups from colleges and universities.

Our contract is with the churches and they are paid \$150 per month for the service of each volunteer. The Mennonites pay their members an allowance of \$10 per month during their first year in the program and \$20 per month during the second year. The Brethren pay an allowance of \$7.50 per month no matter how long the volunteer serves. The people in the program have no complaint about their small allowances. Participation in the program is part of the widespread work conducted as public service by both churches and it extends from helping displaced persons in Europe to aiding migratory workers in California and the southwest.

Every volunteer undergoes an intensive course of basic training

at a church center before reporting for duty at Bethesda. The purpose of this is to weed out anybody who might be mentally or emotionally unsuited for the work to be done in the Clinical Center.

We have an average of from 40 to 50 volunteers with us at all times. They are subject to full hospital discipline and most of them share their rooms with sick patients. They must be on their wards by 9 p.m., and if on pass must return by 11 p.m. If they are on round-the-clock studies, they are not allowed pass privileges.

Life for the volunteers is not as grim as one might imagine when we speak of restrictions. On the lighter side there are group folk dances, the movies and plays that come to the Clinical Center, full use of the gymnasium on the fourteenth floor, and sightseeing in and around Washington. A few attend local colleges two days each week. Others gain useful experience in the laboratories working under the direction of our scientists and technicians, experience that will stand them in good stead when they return to college.

Safeguards Observed

There have been no serious illnesses or deaths since the Volunteer Program began six years ago. The rigid safeguards observed in the Clinical Center are based on the so-called "Ten Commandments" of human medical research which were adopted at the Nuremberg War Crime trials after the atrocities performed by Nazi doctors had been exposed.

Every volunteer must give his or her full consent to every test, and must be told exactly what it involves so that he may know exactly what it involves and go into it with his eyes open.

Among other things, the experiment must be designed to yield "fruitful results for the good of society"; unnecessary "physical and mental suffering and injury" must be avoided; the test must



Art Birk of Teegarden, Ind., receives an intravenous infusion of hormones on an NHI disease research project. Birk is a normal, healthy, young man who has volunteered to serve as a medical research patient. Nurse Lavere Mason and Dr. Grant W. Liddle check up on the procedure.

be conducted by "scientifically qualified" persons, and the subject must be free to end it any time he feels unable to go on. A special board of scientists also studies every projected experiment before it is okayed.

One of the great contributions the volunteers have made has been in the study of drugs. By giving volunteers orinase, one of the new oral drugs for diabetes, scientists were able to determine the effect of different dosages on the blood, the liver, and the kidneys. This has provided vital guidelines for physicians treating patients. It was the same with hydrocortisone, a drug used in skin allergies and other inflammatory conditions.

Take another example. Epinephrine, a hormone produced in the adrenal gland, is one of the most vitally important compounds in the human body. It helps mobilize the body to meet crises by stimulating the heart muscles and increasing cardiac output, boosting blood pressure and spurring the discharge of sugar from the liver into the bloodstream where it can be rushed to tissues and converted into quick energy.

An understanding of how epinephrine works, and how it is metabolized or changed into other chemicals, is vital to the solution of a whole host of problems in medical research. And with the help of volunteers, scientists made a major contribution by working out the chain of chemical events which accompany epinephrine's release in the body.

All in all, the volunteers are performing an important service for medical science which will be reflected in better drugs, better methods of treatment and, occasionally, even cures.

Studies Question Need For Polyoma Virus In Tumor Maintenance

Recently completed studies by Dr. Karl Habel, Chief of National Institute of Allergy and Infectious Diseases' Laboratory of Biology of Viruses, and his associates on the factors responsible for the tumor-producing properties of polyoma viruses have raised a question concerning the necessity for virus presence in maintenance of the tumor. Findings were reported at the meetings of the Federation of American Societies for Experimental Biology, 1960.

Dr. Habel inoculated newborn mice and hamsters with polyoma virus to produce fibrosarcomas which were transplanted into adults of the corresponding species. In the hamster, although virus could be demonstrated in the original tumor, no further evidence for its presence could be found after the first transplant.

Attempts to induce these virus-negative tumor transplants to produce virus in tissue culture under X-ray or ultraviolet radiation failed. On the other hand, in one series of mouse tumor transplants the association of virus with tumor has been consistently positive for 10 transplants.

When virus was given to newborn hamsters, along with antiviral serum at a different site of inoculation, tumors appeared after a longer incubation period. Certain of these tumors apparently were not producing virus, however, since the animals gave no evidence of harboring virus antibodies.

The investigators feel that continuing studies of this nature may help clarify tumor-producing properties in other agents.

Socio-Environmental Factors Seen Related to Addiction

Drug addiction is a complex problem which probably results from multiple factors both within the person and in his social environment. Although there are many unknowns, progress is being made in the understanding of drug addiction.

Knowledge of the life history of addicts, of the impact of socio-environmental factors, and evaluative studies of different methods of treatment are particularly needed.

The recent upsurge of interest in the "tranquilizing" and psychotomimetic drugs has had a stimulating effect on research on narcotic drugs. Increased attention is being given to the basic effects of drug action. Frequently the narcotic drugs are included in investigations focused on the new psychopharmacological drugs.

Considered Chronic Illness

In the area of treatment and rehabilitation of drug addicts, we will probably have to consider drug addiction as a chronic, often intermittent type of illness, like some kinds of mental illness.

It is becoming clear that hospital care alone is not enough and that follow-up, rehabilitative services in the community are essential in the post-hospital period. Here again there is a parallel with current thinking in relation to follow-up services for ex-mental patients.

Tests of the addiction liability of new drugs constitute a major part of the continuing research program of the Addiction Research Center, at Lexington, Kentucky, of the National Institute of Mental Health.

These studies provide information on the human addiction liabilities of drugs (chiefly potent analgesics with morphine-like properties).

This work also evaluates the therapeutic and toxic properties of new drugs for clinical use and provides opportunities for basic research on the mechanisms of tolerance, cross-tolerance, habituation, physical dependence and other aspects of drug addiction.

Testing Difficult

It had been hoped that monkeys might be used as substitutes for humans in the testing of the addictive characteristics of drugs. However, recent studies at the University of Michigan, indicate that some drugs are addictive in monkeys but not in man, while other drugs are addictive in man but not in monkeys. Therefore, it will be necessary to continue the difficult process of using humans in testing addiction liability of new drugs.

Preliminary results from a study carried out by the Institute's Addiction Research Center in which a psychological test (Minnesota

Multiphasic Personality Inventory) was administered to institutionalized narcotic addicts, alcoholics, and criminals indicate that many individuals in all three groups have prominent psychopathic characteristics.

If completion of the study confirms the preliminary results, evidence from psychological tests will be available for the first time to support clinical findings that many addicts have psychopathic personalities. Statistical evaluation is underway to determine whether the personality characteristics of drug addicts can be differentiated from alcoholics and criminals.

Another psychological test, the Addiction Research Center Inventory, is being used in studies of human subjects to measure the subjective effects of drugs.

Empirical Scales Planned

Using the Inventory, it is planned to develop empirical scales for a variety of drugs. This project is of great potential importance, not only because it provides a reliable instrument for quantitative measurement of the subjective effects of drugs, but also because of the opportunities to test basic theories of behavior.

Research workers at Massachusetts General Hospital are attempting to discover how to tell whether or not a person might become an addict if morphine is injected for medical and therapeutic purposes. They have found evidence which suggests that the use of opiates for the relief of pain does not necessarily lead to addiction. In this study, a single injection of morphine in normal persons usually produced a response resembling therapeutic analgesia. This response was different from the effects of morphine in the addict. In the majority of addicts, euphoria was experienced. It appears that there may be personality differences between the potential addict and the non-addict, and further, that this may be demonstrated by a single injection or several injections of an opiate.

Two studies supported by Institute grants are concerned with trying to find out how opium alkaloids (morphine, heroin, etc.) are synthesized in the opium plant. Radioactive tracer techniques are

Leukemic Lesion Found Cause of Fatal Hemorrhage

Dr. Emil J. Freireich and his colleagues of the National Cancer Institute have reported detailed studies of fatal intracranial hemorrhage in patients with acute leukemia whose leukocyte counts rose to more than 300,000 per cu. mm. An earlier paper reported the observation of a distinctive hemorrhagic lesion largely confined to the white matter of the brain in such patients.

In leukemic patients who died of intracranial hemorrhage but whose blood counts were lower than 300,000, the hemorrhage was primarily subdural or subarachnoid, as seen in non-leukemic patients with thrombocytopenia.

Intracerebral nodules of leukemic cells and stasis of leukemic cells (leukostasis) in small intracerebral vessels were found only in patients with leukocyte counts of more than 300,000. Neither leukostasis nor leukemic nodules were found in patients with leukocyte counts below 100,000 per cu. mm.

Vessel Wall Destroyed

The data suggest that local intravascular growth of leukemic cells results in destruction of the vessel wall and formation of a leukemic nodule. Finally, hemorrhage occurs about the nodule and coalescence of many such lesions results in the large hemorrhage seen grossly. This intracerebral leukemic lesion is the major factor responsible for fatal intracranial hemorrhage in patients with high leukocyte counts.

The findings are reported in a recent issue of *Cancer* by Drs. Freireich and Emil Frei, III, General Medicine Branch, NCI; Louis B. Thomas, Pathologic Anatomy Branch, NCI; Richard D. Fritz, now at The Johns Hopkins Hospital; and Claude E. Forkner, Jr., now at Peter Bent Brigham Hospital.

being used to try to isolate the enzyme systems in plants which are capable of synthesizing these complex organic substances.

The synthesis of morphine under these conditions would permit animal studies with these compounds with a radioactive carbon atom in a known position in the molecule. This is exceedingly important for it would permit the pharmacologist to follow what happens to the alkaloid in the animal body.

In other words, it may be possible to localize the areas of the nervous system where the alkaloid or metabolized parts of the alkaloid exert their effects that influence behavior. When we know

Some Virus Antibodies Formed Despite Lack Of Gamma Globulin

Detection of what appears to be naturally acquired neutralizing antibody to polio, ECHO, and Coxsackie viruses in the serum of persons with hypogammaglobulinemia was made in a recent study by Drs. Eugene V. Barnett, John P. Nasou, John P. Utz, and Samuel Baron, of the Division of Biological Standards and National Institute of Allergy and Infectious Diseases.

Despite the characteristic limitation of gamma globulin formation, persons with hypogammaglobulinemia are usually resistant to a second attack of viral infection. Since antibody formation in these patients is usually undetectable by standard tests, resistance generally has been attributed to a non-antibody immune mechanism.

Neutralizing Capacity Found

By a highly sensitive technique (immunoinactivation plaque-neutralization tests), the serums of two patients with congenital hypogammaglobulinemia and of five with acquired hypogammaglobulinemia were found to have neutralizing capacity for a number of enteroviruses.

The plaque-neutralizing material in the serums of these patients has properties of true antibody: 1) It is heat stable, and 2) the reaction of the antibody with the virus is time-dependent—two factors which do not obtain with nonspecific inhibitors.

In a subsequent study, Dr. Baron and co-workers tested the antibody response of four hypogammaglobulinemic patients to a 10-ml inoculation of poliomyelitis vaccine, followed by a one-ml dose one month later. Three of the patients prior to inoculation had low antibody titers to all three types of polio virus.

(See ANTIBODIES, Page 5)

how the body utilizes morphine in the experimental animal, in normal man, and in addicts, we may have crucial leads for devising preventive and treatment methods.

Another biochemical study is related to the efforts of the United Nations to fight the illegal traffic in opium. It is known that opium grown in different regions of the world varies in its chemical constituents.

This project is aimed at developing a method of chemical analysis which can be used to identify the geographical or national origin of a batch of opium. Such information could help to trace the sources of illegal production and sale of opium.

Diamox Produces Parallel Decreases In Venous and Intraocular Pressures

A new technique for studying the effect of Diamox (acetazolamide), a drug used in treating glaucoma, on intraocular and venous pressure in the cat eye has resulted in the discovery of a linear correlation between changes in these pressures. These studies suggest that the vascular system may play a more significant role in maintaining ocular pressure than previously suspected.

A description of the experimental technique and subsequent studies of the effects of Diamox on the eye have been presented by Dr. Frank J. Macri, Ophthalmology Branch, National Institute of Neurological Diseases and Blindness, at the meeting of the American Society of Pharmacology and Experimental Therapeutics.

Correlation Described

A surprising correlation between venous and intraocular pressure in the eye has been described as a result of this new technique for experimentally measuring these pressures without altering the relationship between them. Studies have shown that Diamox produces parallel decreases in both intraocular and venous pressure in the cat eye. Diamox was also found to act selectively, without interfering with the general blood pressure.

Preliminary to the drug study, casts of the aqueous outflow veins of the cat eye were made to demonstrate connections with the systemic veins. The effect of Diamox was then measured by simultaneously recording the aqueous pressure in the anterior chamber and the venous pressure in the anterior ciliary or one of the vortex veins. Continuous measurements were made before, during and after the administration of the drug.

Technique Devised

In previous studies, eye and venous pressure had not been determined simultaneously. Thus the venous pressure was essentially determined on an occluded vein while the eye pressure was obtained under conditions of an unimpaired circulation.

A technique was, therefore, devised where either the anterior ciliary or the vortex pressure was measured simultaneously with the intraocular pressure and the blood pressure. The comparative experiments showed that no changes in the eye's "responsiveness" resulted from the cannulation of veins for purposes of measurement.

When Diamox was administered intravenously, expected decreases in eye pressure occurred. In addition, simultaneous decreases in

eye venous pressure were recorded, which were parallel to intraocular changes in time of onset and in magnitude.

In addition to performing the experiments in living animals, studies were made on isolated arterially perfused eyes. Similar correlations of intraocular and venous pressure were found under this condition and Diamox was still effective in lowering these pressures. Since under these conditions decreases may be ascribed to the alkalinity of the drug used, a comparable buffered solution was administered by continuous perfusion to the isolated eyes. Lack of pressure decreases under these conditions confirmed that Diamox acts directly on the eye.

Pressures Plotted

Intraocular pressures in one eye of each of 39 cats were then plotted against corresponding venous values before and after Diamox administration. Decreases after the use of Diamox were statistically significant for all cases.

A significant linear correlation between venous and eye pressures was found, a relationship which was unchanged by the use of the drug. According to Dr. Macri, this finding could indicate that the vasculature plays a role of greater significance in the maintenance of ocular pressure than has been attributed to it in the past.

Aqueous Inflow Decreased

Although no conclusions are warranted relating to the mechanism by which Diamox causes the venous pressure to fall, two possibilities are indicated:

ANTIBODIES

(Continued from Page 4)

Following inoculation, no significant rise in antibody occurred in two but the third had a small but definite increase to types 2 and 3 after the second inoculation.

The fourth patient had pre-existing antibody to types 2 and 3 polio virus, but none to type 1. Following the first inoculation, extremely small amounts of type 1 antibody were detectable in this patient, which diminished during the third week and increased significantly following the second inoculation. No change in concentration of type 3 antibody was observed.

The result of this second study indicates that hypogammaglobulinemic patients may have a primary or secondary antibody response following exposure to an antigen, but the maximum obtainable antibody levels are severely limited.

One possible interpretation of these findings is that the low levels of antibody in these patients are sufficient to confer immunity to viral diseases but insufficient to confer immunity to many bacterial and fungal diseases.

The study was reported in the *New England Journal of Medicine*.

ibilities are indicated:

Venous pressure may decrease as a result of lowering the eye pressure, since Diamox is known to decrease aqueous inflow. Or, intraocular decreases may be due to falls of venous pressure, implying that some mechanism produces a lessened blood volume.

Further studies on these intricate phenomena may contribute to the understanding of intraocular pressure regulation.

Cytotoxic Effect Of Normal Sera Shown in Tests

Dr. Maurice Landy, of the National Cancer Institute's Laboratory of Chemical Pharmacology, and his colleagues have reported results of a comprehensive study showing that normal serum from human and many other species but not the mouse exerts a lethal effect when mixed in the test tube with mouse tumor cells. This reaction may help to explain why transplants from one species to another do not "take."

An observation that normal serum was capable of exerting cytotoxic effects on tumor cells of heterologous species (species different from that in which serum originated) was reported in the scientific literature many years ago. Recent renewed interest in the possibility that humoral factors participate in the control of tumors has stimulated investigation of the cytotoxic activities of normal serum.

Serum Interacted

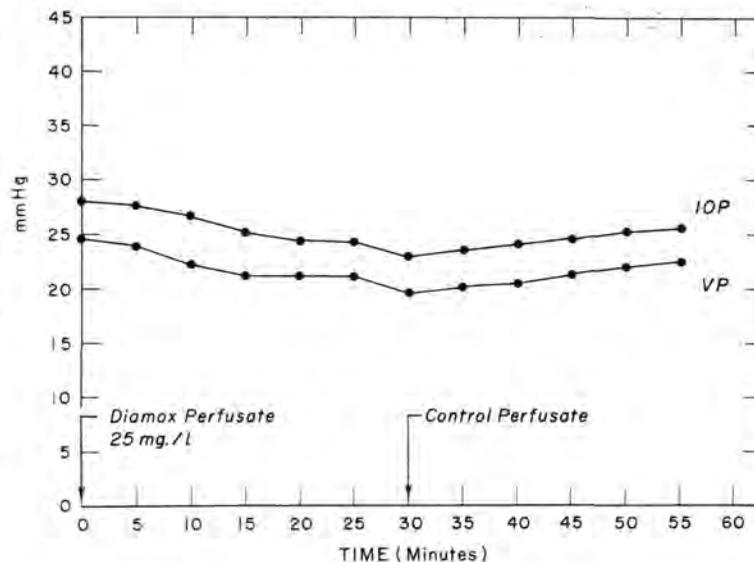
In the present study, human serum obtained from an individual, or pooled by combination of specimens from a number of individuals, was interacted for one hour at 37° C. with Sarcoma 37 ascites tumor cells. Usually one million cells per ml. of serum were used. The cells so treated failed to proliferate in mice, whereas control cells gave rise to progressive growth of tumor within 8 to 12 days. Other evidence of damage by normal human serum to S-37 cells was manifested by their loss of metabolic activity, inability to exclude dyes, and changes in their structure. Of several components in the serum that are responsible for the damaging effect on tumor cells, "normal" antibody is the specific one.

Experiments Conducted

Other experiments were conducted in which the sources of serum and tumor cells were varied. Specimens of serum from 16 other animal species were tested, including chimpanzee, monkey, rabbit, chicken, goat, and sheep. The same damaging effects on S-37 tumor cells were produced by about a dozen of the species examined but not by the others. The reason for this difference is being studied.

Two other mouse tumors, Ehrlich and Krebs ascites, were affected by normal human serum in the same way as were the S-37 tumor cells.

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Effect of Diamox on the enucleated eye: The intraocular pressure and venous pressure can be seen to fall within five minutes after the start of Diamox administration. The fall in both pressures was maximal within 15 minutes and was of similar magnitude. Recovery of both pressures began within a few minutes after reinstating the control perfusion.

Cancer Survival Rates Show Improvement In Quarter Century

Women with cancer of the uterus have a better chance of surviving today than they had 25 years ago, and the improvement may be associated with increased use of surgery in treating this disease.

This is a recent conclusion reached by scientists who have been analyzing data on life expectancy of cancer patients gathered in Connecticut between 1935 and 1954. The investigators suggest that earlier diagnosis resulting from physicians' use of the cytologic, or cell examination, test may also have contributed to the improvement in uterine cancer.

Analysis Published

The analysis, by Sidney J. Cutler and Fred Ederer, of the Biometry Branch of the National Cancer Institute, and Matthew H. Griswold, M.D., and Richard A. Greenberg, of the Connecticut State Department of Health, appears in the current issue of the *Journal of the National Cancer Institute*.

These investigators are preparing a series of reports on survival, three of which have been prepared for publication in the *Journal*. The current issue will include papers on uterine and ovarian cancer; a paper on breast cancer appeared in the issue of November 1959. Future papers in the series will present analyses of survival in cancer of the digestive system and skin.

Data Confirmed

Each of these papers confirms the preliminary analysis of crude data reported in a monograph, "Cancer in Connecticut—1935-1951," which was prepared in 1955 by the Connecticut State Department of Health under a grant from the National Cancer Institute. That study showed that the ratio of cancer patients surviving five years after diagnosis had risen from 1 in 4 at the beginning of the reporting period to 1 in 3 at the end of the period. It also showed that among patients treated surgically for localized uterine cancer, the five year survival rate was nearly 90 percent.

The data that are being comprehensively analyzed consist of the medical records of all cancer patients (more than 75,000) in Connecticut between 1935 and 1954. The figures on survival have been compared with those reported from a number of other treatment centers throughout the country. Because the findings in Connecticut

Decarboxylase Inhibitors Promising In Treatment of Hypertension

Decarboxylase inhibitors, which block the production of aromatic amines suspected of being important in the development of hypertension, are providing a promising new approach to the understanding of this disorder and may eventually provide new means of treatment.

Limited clinical trials of alpha-methyl dopa, the most effective of a new family of compounds called decarboxylase inhibitors, have been conducted by National Heart Institute scientists on ten hypertensive patients at the NIH Clinical Center. The drug lowered blood pressure in all of these patients.

Enzyme Inhibited

Alpha-methyl dopa and related compounds inhibit the enzyme, decarboxylase, whose action is essential to production by the body of norepinephrine, epinephrine, serotonin, and other aromatic amines suspected of playing an important role in hypertension.

Alpha-methyl dopa was synthesized in 1950 by Drs. G. A. Stein, H. A. Bronner, and Karl Pfister of the Merck Sharp & Dohme Research Laboratories Division of Merck & Co., Inc., Rahway, New Jersey.

Clinical trials of the drug were conducted by Drs. Albert Sjoerdsma, Louis Gillespie, J. R. Crout, and J. A. Oates, of the Laboratory of General Medicine and Experimental Therapeutics, following biochemical work by Dr. Sidney Udenfriend, of the Laboratory of Clinical Biochemistry. Their findings were reported by Dr. Oates at the American Society for Clinical Investigation meeting in Atlantic City.

were virtually identical with those reporting elsewhere, they are considered to be representative of the entire United States.

The investigators report that survival in ovarian cancer has not improved significantly in the last 25 years. In both ovarian and uterine cancer, the outlook for younger women is better than that for older women.

Survival among breast cancer patients also has not changed significantly in the past quarter century, nor have incidence and mortality for this disease. The investigators conclude that any future improvement in breast cancer survival is more likely to come from the development of new techniques than from refinement of current methods of treatment.

The findings indicate that alpha-methyl dopa holds promise as a research tool, not only in hypertension, but also in other diseases (such as malignant carcinoid) that are characterized by excessive levels of certain aromatic amines. The scientists also feel that alpha-methyl dopa and its relatives show sufficient promise in the treatment of these disorders to warrant extensive therapeutic evaluation.

Amines are synthesized from amino acids supplied by dietary protein. Like all organic acids, amino acids are characterized by the presence on their molecules of one or more carboxyl (-COOH) groups. An essential step in the synthesis of amines is the removal of the carboxyl groups of their amino acid precursors by the action of decarboxylase. Alpha-methyl dopa and its relatives block amine production by inhibiting this enzyme.

Amine Production Blocked

Certain amines, notably norepinephrine and epinephrine, are known to be important in blood pressure regulation and have also been suspected of being villains in hypertension. Therefore decarboxylase inhibitors, which block the production of these amines, are of great scientific interest both for the light they might shed on the underlying causes of hypertension and for their possible use as therapeutics.

Alpha-methyl dopa has been found to block amine production in man, but whether this action is the key to its hypotensive action is uncertain. Other effects of the drug—tranquilization and sedation—also require further study. These and other effects appear to diminish with continued treatment.

SERA

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In addition, cells of about a dozen mouse and rat tumors were found to be capable of absorbing the "normal" antibody from human serum, proving that this antibody is not specific for any individual tumor. Furthermore, lymphoid tissues of mice—spleen, lymph nodes, thymus, and bone marrow—also absorbed the antibody. These findings suggest that the various tumors and lymphoid tissue, which absorb the antibody, possess a common antigen.

The number of cells that could be killed by a standard dose of serum was impressive. Intracerebral injection of as few as 30 S-37 cells could produce tumors. In contrast, 500,000 cells that had

Flouride Tablets Reduce Decay in Non-Communal Water Supply Areas

Although the fluoridation of public water supplies has become an accepted dental health procedure, one-third of the U.S. population does not have access to communal water supplies and may never reap the benefits of this discovery. For this group one of the alternate means of adding fluorides to the diet, which has received considerable attention, is the use of fluoride tablets.

Dr. Francis A. Arnold, Jr., Director, National Institute of Dental Research, recently presented results of a long-term study of caries inhibitory effects of fluoride tablets in children. Conducted with Dr. F. J. McClure, Chief, Laboratory of Biochemistry, NIDR, and Carl L. White, NIDR statistician, the study concluded that the one-a-day tablet regimen could have a beneficial effect on the teeth of growing children.

Fluoride Levels Comparable

The mean numbers of DMF (decayed, missing, or filled) and DEF (decayed, extraction indicated, or filled) teeth of 121 children ingesting a daily fluoride tablet were compared with corresponding data previously reported for children using natural fluoride or fluoride-adjusted drinking water. Cario-static effects of the two procedures appeared to be of generally comparable levels. The tablets, containing 2.21 mg. of NaF (1.0 mg. of fluoride) did not appear to cause any cosmetically significant fluorosis.

Method Effective

The mean fluoride content of deciduous teeth of children ingesting these tablets was found to be higher than that of children in a non-fluoride area. It also appeared that the fluoride content of teeth increased proportionately with the length of time the tablets were ingested.

Based on data gained during the test program, the investigators concluded that the tablet method, while effective, is not as practical as water fluoridation. Further, the fact that the fluoride content of the "home" water supply must also be known suggests that as a public health procedure this method could best be used in controlled programs supervised by health authorities.

been interacted with 1/20 ml. of human serum produced no tumors.

The investigators conclude that there is "widely distributed among animals a type of 'natural' antibody, which . . . may serve as a barrier against invasion by cells of foreign species."

The NIH Spotlight

By Kathryn Mains

Turning his back on Washington's beautiful, if belated, springtime, Dr. Leon Jacobs, in the interests of science and good international relations, is heading toward the chilly New Zealand winter that begins in June.

Chief of the Laboratory of Parasitic Diseases, NIAID, Dr. Jacobs has been awarded a Fulbright Fellowship to work at the Wallaceville Animal Research station in



Dr. Leon Jacobs

collaboration with scientists of the New Zealand Department of Agriculture.

He will study the problem of toxoplasmosis, particularly in sheep. As many as 15 percent of newborn lambs are lost on some properties in New Zealand because of infection of the ewes with this disease. This is a problem of considerable importance in a country of two and a half million people whose primary export is wool from more than 34 million sheep.

Through research and the teaching of improved serologic technics for diagnosis of toxoplasmosis, which he has perfected here, Dr. Jacobs hopes to help improve this situation. He has planned a practical research program which will include investigations on transmission and pathogenesis, as well as serodiagnosis of toxoplasmosis. From this he expects to learn while teaching, during his nine-months fellowship.

Dr. Jacobs' wife and three children are going with him to New Zealand, where a house is ready for them in Upper Hutt, near the capital city, Wellington.

The New Zealand working experience will be something of a novelty for Dr. Jacobs whose entire professional career has been centered at the National Institutes of Health. He began work in the laboratory in 1937 as a junior scientist in the Division of Zoology when it was at 25th and E Sts. Now the head of a laboratory with a staff of 36, he remembers when the entire Division of Zoology,

U.S., Soviet Physicians Here For Talks on Heart Disease

Four Soviet scientists visited the National Heart Institute early this month for official discussions on plans for a U.S.-U.S.S.R. program of scientific cooperation in the field of heart disease.

The visit was made under the Health and Medical Section of the U.S.-U.S.S.R. Exchange Agreement signed last November.

The first four days of the visit, May 9-12, were spent at NIH, where the Heart Institute staff was host to the group. Discussions were held on atherosclerosis, hypertension, anticoagulants, cardiovascular surgery, and other topics of mutual interest.

The Russian party, headed by Dr. Alexander Myasnikov, Director of the Institute of Therapy, Academy of Medical Sciences, Moscow, included Dr. Ivan Speranskiy and Dr. Mariya Bavina of the same Institute, and Dr. Nodar Kipshidze, Professor and Head of the Faculty of Therapy Clinic, Tbilisi.

The U. S. participants, headed by Dr. James Watt, NHI Director, included Dr. Luther L. Terry, Assistant Director, NHI; Dr. Paul D. White, Harvard Medical School; Dr. E. Cowles Andrus, Johns Hop-

kins Hospital; Dr. Michael E. De Bakey, Baylor University; Dr. Irvine H. Page, Cleveland Clinic; Dr. David D. Rutstein, Harvard University Medical School; Dr. Robert W. Wilkins, Boston University School of Medicine; and Dr. Irving S. Wright, Cornell University.

The group spent May 13 in Baltimore touring the NHI Gerontology Laboratory at the Baltimore City Hospitals, and the Johns Hopkins Hospital and Medical School. During the following week they visited scientific institutions in Boston, Cleveland, and New York.

Discussions held during the Soviet scientists' visit will, it is hoped, facilitate contacts between the two countries in the field of cardiovascular disease, including: 1) the exchange of information about research now being conducted and planned, 2) the organization of joint scientific studies, 3) the exchange of specialists, and 4) joint participation in yearly scientific meetings.

Other scientific exchanges are planned between research organizations conducting studies on the problems of cancer, poliomyelitis, and other important problems of medicine.



Soviet heart specialists are greeted by NIH officials on their recent visit here for conferences. From left: Drs. Nodar Kipshidze, Mariya Bavina, James Watt, NHI Director; Alexander Myasnikov, Ivan Speranskiy, Luther L. Terry, NHI Assistant Director; and James A. Shannon, NIH Director.

forerunner of NIH, numbered 18, with himself its most junior member.

Twenty-three years later (including three years of military service during World War II), Dr. Jacobs vividly recalls the early days of life at NIH. He remem-

bers when building space was not the problem it is today, and meetings were small and quite informal.

The NIH scientific staff held a single seminar followed by cookies and tea in the Director's office. "A little crowded, as I recall," says

Virology Studies Win Lilly Award For Dr. Rowe

Dr. Wallace P. Rowe of the Laboratory of Infectious Diseases, NIAID, has won the Eli Lilly & Co. Award in Bacteriology and Immunology.

Dr. Rowe received the award, consisting of a bronze medal and \$1,000, at the annual meeting of the Society of American Bacteri-



Dr. Rowe

ologists in Philadelphia the first week in May.

This award is given each year to a scientist younger than 35 years of age who has contributed significantly in

the broad field of bacteriological research.

In 1936, the first year it was presented, the award went to Dr. Harry Eagle, also of NIAID.

Dr. Rowe, a virologist, is the senior author of the first published paper in the scientific literature describing the new group of viruses identified as adenoviruses.

He has also been prominently associated with Dr. Robert J. Huebner in the study of many virus problems, most recently concerning the polyoma virus.

Since 1952 when he joined Dr. Huebner's staff, Dr. Rowe has been co-author of over 50 papers on laboratory and clinical aspects of viral research.

A Commissioned Officer, Dr. Rowe is Chief of the Oncolytic and Oncogenic Virus Unit of the Virus Section, LID.

Dr. Jacobs, "but we did all fit in one room."

He remembers the Division of Zoology as a small, friendly unit with an *esprit de corps* that was a credit to its long-time chief, Dr. Willard H. Wright, who retired from the PHS Commissioned Corps just two years ago.

And he remembers when the media room at 25th and E served a vital supplementary function. In the absence of a cafeteria, homemade vegetable soup was concocted there in a huge pot and sold at lunchtime for 10 cents a bowl.

After the war, during which he earned an Army commendation for work as Malaria Control Officer at U. S. Army Headquarters in the South Atlantic, in Recife, Brazil, Dr. Jacobs returned to NIH and finished graduate studies at night to earn his Ph.D. in Zoology. In 1948 he joined the Commissioned Corps, in which he now holds the rank of Scientist Director.

Biomedical Engineering Is New Interest Field

The first annual symposium on educational frontiers in biomedical engineering was held May 5-6 at the University of Vermont.

Biomedical engineering, a new curriculum leading to graduate degrees in several universities, including Yale, Columbia, and Johns Hopkins, provides for the cross-fertilization of education in biology, medicine, and engineering.

The symposium brought together students, teachers, and representatives of industry, government, and education who are interested in advancing this new field of medical science.

NIH was represented by Grant C. Riggle, Chief of the Electronic Engineering Unit, Instrument Engineering and Development Branch, DRS, program chairman; Dr. Peter L. Frommer, Laboratory of Technical Development, NHI, and Dr. Mathilde Soloway, Research Grants Branch, DGMS. They participated in panel discussions on research opportunities in medical instrumentation.

The symposium was sponsored by the National Science Foundation, the American Institute of Electrical Engineers, the Institute of Radio Engineers, and the University of Vermont.

Credit Union Announces Semi-Annual Dividend

The Board of Directors of the NIH Federal Credit Union has announced the forthcoming payment of a semi-annual dividend and the appointment of a new manager.

The amount of the dividend will be announced in June. It will be paid in July for money on deposit as of June 30. In addition, all money deposited by the fifth day of any month will earn dividends for that month.

O. J. Wood, former manager of the Washington Telephone Federal Credit Union, has been appointed manager of the NIH Federal Credit Union. He succeeds Zella N. Boteler.

SMB Bulletin Series Aids in Requisitioning

Supply Management Branch recently announced the publication of a new information bulletin series, titled the *SMB Information Bulletin*, "to meet the need for better communication between this branch and other areas of NIH."

The bulletins are pre-punched and issued in the form of General, Procurement, Property and Supply, and Research Contracts releases.

Published in two colors—white for information of a permanent nature and yellow for temporary issuances—the bulletins are distributed to all Executive and Ad-

Liaison Representatives Are Listed Here

Following is a list of the Liaison Representatives who will coordinate the Federal Employee Health Benefits Program throughout NIH. If an employee does not receive an information kit or is unable to determine whether he is eligible for enrollment, he should contact the Liaison Representative of his Institute or Division.

Area	Representative	Bldg.	Rm.	Ext.
OD	Genevieve Garner	1	138	2511
DBS	W. J. Stalters	8	216	833
DGMS	Anne Udoff	16	208	4418
DRG	H. W. Curran	T-6	1011	4458
DRS	R. H. Handy	1	309	4501
CC	Edward F. Zadal	10	1N216	3227
NCI	H. Ken Painter	T-19	104	801
NHI	P. Janus	3	104	2419
NIAID	J. M. Hannan	10	11N314	847
NIAMD	E. J. Liljegren	10	9N202	3225
NIDR	J. E. Fitzgerald	2	107	715
NIMH	C. E. Miller, Jr.	T-18	105	4153
NINDB	H. Jeni Arliss	8	118	2576

REGISTRATION

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Benefit Plan, and the Group Health Association Plan.

A fourth brochure, describing the Employee Organization Plan, which is available only to members of the American Federation of Government Employees, will be sent directly to those who are eligible for enrollment. Additional copies of this fourth brochure are available for review in the Personnel Management Branch, Bldg. 1, Rm. 21, and in Bldg. 10, Rm. 1S229.

The nation-wide Federal Health Employee Benefits Program becomes effective at NIH July 10. The Personnel Management Branch reminds employees that under each of the four plans the portion of the premium to be paid by the employee will be deducted from each of his paychecks in equal amounts throughout the year. The first deduction will be reflected in the paychecks of August 2.

PMB also calls attention to the fact that any employees who do not enroll in one of the four plans during the forthcoming registration period will not have an opportunity to enroll again until October 1961.

Since there is a wide choice of plans, and a selection of benefits within each of the plans, employees are urged by PMB to study the brochures carefully before reaching a decision.

Under each of the four plans, PMB points out, a medical certification is required for children over age 19 and a dependent husband enrolled on a family contract who are incapable of self-support. This medical certification must be ob-

ministrative Officers, to Division and Branch Chiefs, and to other requisitioning points.

For additional copies or to be placed on the mailing list, call Office of the Chief, SMB, Ext. 2315.

tained from the employee's own physician, at his own expense, and must be attached to the registration form.

Information required for this medical certification is included on HEW Form 572, "Certification of Incapacity," available through the Registration Assistants.

PMB also urges employees to take good care of the brochures descriptive of the several insurance plans, because "the brochure of the plan selected is the employee's contract."

Ineligibility Listing

Following is a list of exclusions specified by the Civil Service Commission, under which employees are *not* eligible to enroll in any one of the Health Benefit plans.

1. Employees serving under appointments limited to one year or less, except employees so appointed for full-time employment without break in service or after a separation of three days or less, following service in which they were enrolled under this part, and acting postmasters.

2. Employees whose employment is of uncertain or purely temporary duration, or who are employed for brief periods at intervals, or who are expected to work less than six months in each year.

3. Employees in the postal field service serving under temporary appointments pending establishment of a register.

4. Part-time, when-actually-employed, or intermittent employees having no regular tour of duty.

5. Employees whose salary, pay, or compensation on an annual basis is \$12 a year or less.

6. Beneficiary or patient employees in Government hospitals or homes.

7. Employees paid on a contract or fee basis.

8. Employees paid on a piece-work basis, except those whose work schedule provides for regular or full-time service.

Ora Marshino Retires; Was With NCI in '37

Miss Ora Marshino, who was administrative assistant in the National Cancer Institute at the time of its establishment in 1937, retired from Government service May 4 to join the staff of the Research Division of the Republican National Committee.

At the time of her retirement—the second of her Government career—Miss Marshino was serving as program analyst in the Office of the Director, NCI. Previously she had also worked for seven years in the Information Office of the Institute.



Miss Marshino

Following her earlier retirement, in 1954, Miss Marshino worked part-time for NCI as a writer of special reports, and during 1956 was a research analyst in health, education, labor and welfare for the Republican National Committee.

Returning to NCI in 1957, Miss Marshino assisted in the preparation of the 20th anniversary issue of the *Journal of the National Cancer Institute*, and prepared an extensive 20-year report of the NCI research fellowship program.

A member of the American Bar Association and the Women's Bar Association of the District of Columbia, Miss Marshino received a law degree from The George Washington University in 1937. She also holds an A.B. degree and an M.A. in political science from G.W.U.

Revised Bus Service In Effect on June 1

Starting Wednesday, June 1, all shuttle buses from NIH to the Robin Building and DHEW will start from the main entrance of the Clinical Center.

The DHEW shuttle service will be non-stop, reducing the trip time from one hour and 10 minutes to 40 minutes, and increasing the number of daily trips by four.

To make reservations on the DHEW shuttle and for schedule information, call the CC receptionist, Ext. 3141.

The Robin Building shuttle will stop at Buildings T-6 and T-19. Passengers commuting between the Robin Building and DHEW must transfer at the Clinical Center. Reservations are not necessary on the NIH-Robin Building shuttle.

The new schedule is available from Administrative Officers and the CC receptionist.