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HEALTH, EDUCATION, AND WELFARE

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NIH Investigators Report Research At ACP Session

Internists from all parts of the United States are in Miami Beach this week for the Forty-Second Annual Session of the American College of Physicians, scheduled to begin yesterday and continue through Friday.

Among the more than 100 scientific papers to be presented at the 5-day meeting were nine reporting the research findings of 22 NIH scientists. A paper by five physicians engaged in the NHI-supported Heart Disease Epidemiology Study at Framingham, Mass., will report on "Six Year Follow-up Experiences."

Kornberg to Speak

The program includes basic medical science sessions, clinical sessions and conferences, and panel discussions in which five NIH staff members are participating.

Special lectures are being presented by Drs. Arthur Kornberg of Stanford University, the 1959 Nobel Prize Winner in Medicine and former Chief of NIAMD's Enzyme and Metabolism Section; Armand L. Quick, Marquette University School of Medicine; and Sir Robert Platt of the University of Manchester,

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More Support, Expansion of Research Urged by Heart-Cancer Conference

More Federal and voluntary support of all medical research, including that in heart disease and cancer, was one of the chief recommendations of the President's Conference on Heart Disease and Cancer which presented its report at the White House on April 21.

"We enthusiastically endorse," the conference report said, "the conclusion of the President's Health Message which states that there should be a vast expansion of medical research."

The conference had been requested by President Kennedy five weeks earlier.

The report pointed out that, "The magnitude of the funds required

HEW Secretary to Dedicate New NIDR Building May 26



Architect's sketch of the new Dental Institute Building.

A large number of distinguished guests, including DHEW Secretary Abraham Ribicoff, members of Congress, Government leaders, and representatives of the dental profession and related biological and medical fields, will gather here May 26 to participate in ceremonies dedicating

the new \$4 million building of the National Institute of Dental Research.

Located on South Drive opposite the Clinical Center, the 5-story laboratory-office building is essentially of the same design and construction as the Division of Biologics Standards Building, dedicated last June.

Ceremonies Start at 2 p. m.

It will provide much needed research facilities for the expanding Institute which has grown from 30 employees at its founding in 1948 to over 200 at the present time.

The dedication ceremonies are scheduled to begin at 2 p.m. in the area in front of the building. In event of rain they will be held in the CC auditorium.

Dr. Luther L. Terry, PHS Surgeon General, will deliver the welcoming address. The principal guest speaker will be Dr. Emory W. Morris, President and General Director of the W. K. Kellogg Foundation, which has made outstanding contributions in the fields of dental education and research.

The program participants will include Sen. Lister Hill of Alabama, Rep. John E. Fogarty of Rhode Island, Rep. Melvin R. Laird of Wisconsin, Dr. Charles H. Patton, President of the American Dental Association; and Dr. James A. Shannon, NIH Director.

Dr. Francis A. Arnold, Jr., NIDR

Science News Placement Changed in Policy Shift

Beginning with this issue, the summaries of research findings reported by NIH scientists, which previously have been published in the 4-page Science Section of the *Record*, will be carried, together with news of interest to all NIH employees, throughout the pages of the *Record*, as their relative importance appears to warrant.

NIAID Scientists Open New Vistas To Allergy Studies

For the first time, allergic thyroiditis has been produced experimentally in a strain of inbred guinea pigs. This study and definition of the underlying mechanisms of autoimmune disease in experimental animals has opened new vistas for understanding the human autoimmune diseases, among them one form of human thyroid disease.

The research was conducted in the National Institute of Allergy and Infectious Diseases by Dr. Phillip R. B. McMaster, Dr. Edwin M. Lerner, II, and Eurnal D. Exum.

Provide Model

The so-called autoimmune or autoreactivity diseases are believed to occur when an individual becomes allergic or sensitive to substances present in his own body. Immunologic reactions may occur between altered tissues or tissue products of the individual and his own defense mechanisms, which no longer recognize these tissues as belonging to the individual.

The findings provide a model for further study of Hashimoto's thyroiditis, believed to be an autoimmune disease, and some forms of hemolytic anemia. Other human diseases such as rheumatoid arthritis may be caused by immunologic reactions.

Identical Strains Used

An allergic inflammation of the thyroid was induced in Strain 13 guinea pigs by injecting them with extracts of thyroid glands of other guinea pigs of the same strain. Since animals of this strain are so immunologically similar that they readily accept skin grafting from one another, there was no possibility of a natural defense reaction to foreign tissue.

The extracts were mixed with Freund's adjuvant, a substance which intensified immunological response. The disease appeared in some animals as early as five days after injection. This is the earliest

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the Record

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Editor.....E. K. Stabler
Associate Editor.....Elizabeth D. Eberhard

Staff Correspondents

Sandra Polsky, NCI; Patricia L. Spencer, NHI; Kathryn Mains, NIAID; Lillie Bailey, NIAMD; Marie Norris, NIDR; William Gray, NIMH; Pat MacPherson, NINDB; Elsie Fahrenthold, CC; Mary Henley, DBS; Corinne Graves, DGMS; Shirley Barth, DRG; Jean Torgerson, DRS.

PERSONNEL TO PERSON

ALL NIH Civil Service employees will soon be requested to give their Social Security numbers to Personnel Management Branch.

These numbers will be used by the CSC in their improved personnel statistics program which will go into effect later this year.

This does not mean that the Social Security Act is being extended to cover Government employees. The number will be used only for identification.

The mechanics of collecting the numbers of NIH employees will be announced shortly. Employees who do not have Social Security numbers will be provided with the necessary forms to acquire them.

HEALTH BENEFITS SURVEY

Preliminary data from the CSC's Health Benefits survey indicates that the majority of Federal employees are satisfied with the 10-month-old program but would like to see certain changes made.

Early returns from short questionnaires being filled out anonymously by 1 out of every 10 employees show that: ninety percent of all employees would stay with their present plans, more than a third have actually used their plans since the program started last July, four out of every five employees who have used their plans were satisfied, and about one-third of the employees who have filled out questionnaires suggested specific changes in their present plans, and about one-fifth suggested changes in the overall program.

Complaints Cited

Major complaints of the "dissatisfied users" concern delays in paying claims, difficulties with forms and procedures, and the belief that the plans don't pay enough for what they cost.

The overall program changes

Soviet Pharmaceuticals Described in New Index

A Russian Drug Index, containing a comprehensive listing of drugs currently in use in the Soviet Union for therapeutic and experimental purposes, was published recently by the National Library of Medicine.

It is designed to overcome obstacles to understanding Russian scientific literature presented by the language barriers, since Russian drug names often have no relation to the generally accepted names used for medical purposes in other parts of the world.

Entries are listed alphabetically by subject. A typical entry contains the anglicized name of the drug in capital letters, a transliterated Russian name in parentheses, a chemical formula or composition, a structural formula, a short description of drug properties, a Russian source, and an American bibliographic reference when available.

The Index—PHS Publication No. 814—may be obtained from the Superintendent of Documents, U.S. Government Printing Office, Washington 25, D.C., at 60 cents a copy.

most frequently requested so far would: give employees more detailed and specific information, provide a Government contribution for married women whose husbands are non-dependent (equal to the contribution for other married employees), and to establish special, reduced rates for certain groups, such as small families and older couples beyond the child-bearing age.

The Commission emphasizes that these are preliminary findings and that later returns may give a different picture.

The returns are being reviewed as rapidly as possible so that they can be used in negotiations for new contracts and in planning for better, faster service to enrolled employees.

Police Foil Daytime Payroll Robbery, Capture Gunmen on the Reservation

By Ken Stabler

Until they read about it in their newspapers or heard it on the air, only a handful of NIH employees were aware that the reservation had been the scene of gunplay resulting in the capture of two alleged payroll bandits here on Friday, April 28.



The Montgomery County policemen who frustrated the payroll robbery and captured two gunmen on the NIH reservation stand beside their scout car. Pvt. Duane Van Dusen (left) shot one of the gunmen in the foot. Pvt. Demetrius Kaponin points to bullet holes in the car window caused by shots he fired at the other man.—Photos by Jerry Hecht.



Thomas M. Burford, plasterer company foreman who was held up and robbed of the company payroll, leaves the Bethesda Police Station after questioning by police and the FBI.

ACP SESSION

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England, and President of the Royal Society of Physicians.

A special feature of this year's session is the closed circuit telecast of medical and hospital clinics, taking the place of clinics held in hospitals.

In conjunction with the meeting, a technical exhibit displays the products of 97 equipment and drug manufacturers. Six non-commercial organizations, including DHEW, also have exhibits at the meeting.

The gunmen were subdued and arrested in the rear of the 11-story Office Building under construction here, after the firing of five shots by two Montgomery County policemen who had followed them from Bethesda in connection with a minor traffic violation.

During the brief set-to, in which the police used their guns to prevent the men's escape, one of the officers was pistol-slugged on the head and one of the suspects was shot in the foot. Both were taken to Suburban Hospital for treatment.

Capture of the two men—Dorset C. Calp, 37, and Roy E. Calhoun, 30, both of Baltimore—climaxed a bizarre daytime holdup attempt in the busy central area of Bethesda.

Foreman Is Victim

The victim was Thomas M. Burford, 40, foreman of the E. L. Thompson Co., Atlanta, Ga., plastering subcontractor on the Office Building project.

According to police, this is what happened:

Burford, driving a company pickup truck, went to the Bethesda Post Office shortly before 11 a.m. to get the firm's payroll, consisting of \$7,628.95 in cash and \$171.19 in checks.

Carrying the money in a canvas bag covered with a layer of sandpaper, he got in the truck, parked nearby, and was about to step on the starter when the two gunmen appeared.

Stopped by Police

He was ordered to move to the middle of the seat and the two men climbed in, one on each side, Calp behind the wheel and Calhoun nudging him in the ribs with his automatic.

At the intersection of West Lane and Montgomery Lane the truck drove through a stop sign. The traffic violation was observed by Pts. Duane Van Dusen and Demetrius Kaponin who at that point happened to be about half a block behind the truck in their scout car.

They overtook and stopped the truck on East Lane, a short distance from Wisconsin Avenue, and asked the occupants to show their registration card. Burford, in the center with a gun in his side, said the truck owner had the registration in his construction office at NIH.

The police then told the men to drive there, and followed them out Wisconsin Avenue and onto the

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Noted Scientist From Philippines Confers at NIH

Dr. Paulino J. Garcia, Chairman of the National Science Development Board of the Philippine Islands, conferred with Dr. Shannon and other NIH administrators during a visit here April 20. He also inspected areas of the Clinical Center.

Dr. Garcia is visiting scientific institutions and talking with research administrators in this country relative to the planning of a broad program of scientific research and development for his homeland in the years immediately ahead.

Discusses Research Plans

At a luncheon in the NIH Director's office, Dr. Garcia discussed the planning of research programs on a national scale with Dr. Shannon, Dr. David E. Price, NIH Deputy Director; Dr. Kenneth M. Endicott, NCI Director; Dr. Carl Baker, NCI Associate Director for Program; and Robert H. Grant, Assistant Chief of the new NIH Office of International Research.

Dr. Garcia, who was Secretary of Health in the Philippine Cabinet from 1953 until his appointment as Chairman of the National Science Development Board, was accompanied by Dr. Ricardo Cruz, NSDB Supervising Scientist, and Conrado Ramirez of the Philippine Embassy.

Dr. Baker met the visitors at the PHS Surgeon General's office and escorted them to NIH. He remained with them during the discussions in Dr. Shannon's office and later, with Dr. Endicott and Mr. Grant, accompanied them to the Clinical Center

NOL Honors Pearlman For Electronic Device

William Pearlman, an electronics engineer in the Instrument Engineering and Development Branch, DRS, recently received a superior accomplishment award from the U. S. Naval Ordnance Laboratory for his invention of an amplitude comparator circuit.

The Office of Naval Research intends to apply for patent protection of the invention, which is a highly sensitive device used for testing electronic assemblies in underwater mines.

The Navy holds patents on other inventions of Mr. Pearlman developed during his employment with NOL. The invention that led to the recent award employs a technique sometimes used in nuclear electronics to automatically compare, amplify, and measure minute differences between an alternating current signal and a direct current reference voltage.

Mr. Pearlman was with the Army Signal Corps at Fort Monmouth, N. J., and the Naval Air Development Center at Johnsville, Pa., before coming to the Washington area.

He is presently engaged in studies involving radio frequency instrumentation.

where Dr. Robert Farrier, CC Assistant Director, joined the group.

Dr. Garcia, whose distinguished public service career is recognized in this country as well as in his homeland, was said to have expressed a strong interest in the possibility of Philippine research administrators spending some time in this country in order that they might learn methods of operations in United States research organizations.



Representatives of the Philippine Islands are greeted on arrival here in front of the Administration Building by Drs. Shannon and Price, Director and Deputy Director of NIH. Left to right: Dr. Price, Dr. Ricardo Cruz, Supervising Scientist of the Philippine National Science Development Board; Dr. Paulino J. Garcia, Chairman of the NSDB; Dr. Shannon, and Conrado Ramirez of the Philippine Embassy.

New Hypothesis Presented On Permeability of Cells

Using a one-molecule-thick layer of lipoidal molecules and observing the interactions on this system of two antagonistic classes of drugs, Dr. A. M. Shanes and his colleagues in the Laboratory of Pharmacology and Toxicology at NIAMD have been able to develop new concepts on the passive transport of ions in and out of cell membranes and to produce the first new working hypothesis in many years on the nature of these permeability changes.

Dr. Dunn, NCI, Is First Woman to Head AACR

Dr. Thelma B. Dunn, Head of the Cancer Induction and Pathogenesis Section of the National Cancer Institute's Laboratory of Pathology, has been elected President of the American Association for Cancer Inc.



She is the first woman in the history of the Association to serve as its president. She was vice president of the Association last year.

Dr. Dunn came to NIH in 1942 as a Research Fellow in the National Cancer Institute and was appointed to her present NCI post in 1950.

Dr. Dunn received her M.D. degree from the University of Virginia Department of Medicine in 1926 and subsequently served as instructor and assistant professor of pathology at that institution and as a research assistant in pathology at George Washington University.

She was one of six U. S. women chosen to visit the U.S.S.R. in May 1958 as a member of the Delegation of American Women Physicians to Russia. In 1959 she was named "Woman of the Year" by the District of Columbia Branch of the American Medical Women's Association.

Dr. Goldberg to Leave NIH for Emory Post

Dr. Leon I. Goldberg of the National Heart Institute Experimental Therapeutics Branch leaves NIH July 1 to become Associate Professor of Pharmacology and Assistant Professor of Medicine at Emory University, Atlanta, and to establish a Section of Clinical Pharmacology within the Emory University Department of Medicine.

Dr. Goldberg has been a Clinical Associate at the Heart Institute since 1958. Among his present studies are laboratory and clinical investigations of drugs used in the treatment of hypertension and angina pectoris. He is also a member of the editorial board of the Journal of Pharmacology and Experimental Therapeutics.

An important feature of many excitable cells, such as those found in nerve, brain and heart tissue, is that their permeability to ions and large molecules depends on the electrical potential difference or the strength of the electrical field across the outermost boundary of the cell known as the membrane. Thus, in nerve fibers the decrease in this potential difference (depolarization) leads to a short-lived increase in sodium permeability, often followed by a slower development of a temporary increase in potassium permeability.

Clues Provided

Important clues on the permeability mechanism have been provided by research on the monomolecular films of fat-derived molecules. It has been shown that agents such as local anesthetics, which belong to a class of compounds called "stabilizers," interact with the films so as to increase packing of molecules—an effect reflected by increased "surface pressure." Conversely, another group of agents, called "labilizers" or "unstabilizers" (veratrine alkaloids), reduce the surface pressure when the film molecules are tightly packed by removing some of these molecules—an effect antagonized by stabilizers and other agents that antagonize the labilizers in living systems.

Stabilizers Interact

From experimental evidence, Dr. Shanes has concluded that stabilizers interact with molecules surrounding sites of ion passage in the resting or excited membrane. Low concentrations of these agents may not raise the surface pressure sufficiently to interfere with the passage of the ions in the absence of excitation, but sufficient to interfere with an increase in permeability, such as occurs during excitation. The increase in permeability to ions produced by labilizers is interpreted from the monolayer results as the consequence of removal of one or more lipid molecules that surround the sites of ion passage.

Thus, these studies provide the view that the permeability to ions

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New Hypothesis Presented

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is inversely dependent on the packing of molecules of the membrane or on the related surface pressure.

This view has, in turn, been extended in an effort to explain the dependence of membrane permeability on the potential difference across the cellular membrane. As already mentioned, natural membranes are usually subjected to a strong electric field—about 100,000 volts per cm.; the inner boundary is normally negative and the outer boundary positive.

Outer Boundary Affected

Dr. Shanes proposes that the membrane contains charged organic molecules which, by virtue of being much more soluble in the membrane than in the surrounding aqueous solutions, remain in the membrane but with the positively charged ions (cations) pushed by the electric field towards the inner boundary of the membrane and oppositely charged anions towards the outer boundary. There is evidence, from Dr. Shanes' and other laboratories, that the outer boundary of the membrane is the zone which undergoes the permeability changes. Consequently, the concentration of organic cations and anions in contact with this zone is suggested to control the permeabilities to sodium and potassium. Thus, when there is a decrease in the potential difference across the membrane the anions drift away from this region, thereby increasing sodium or potassium permeability. The cations, mainly at the

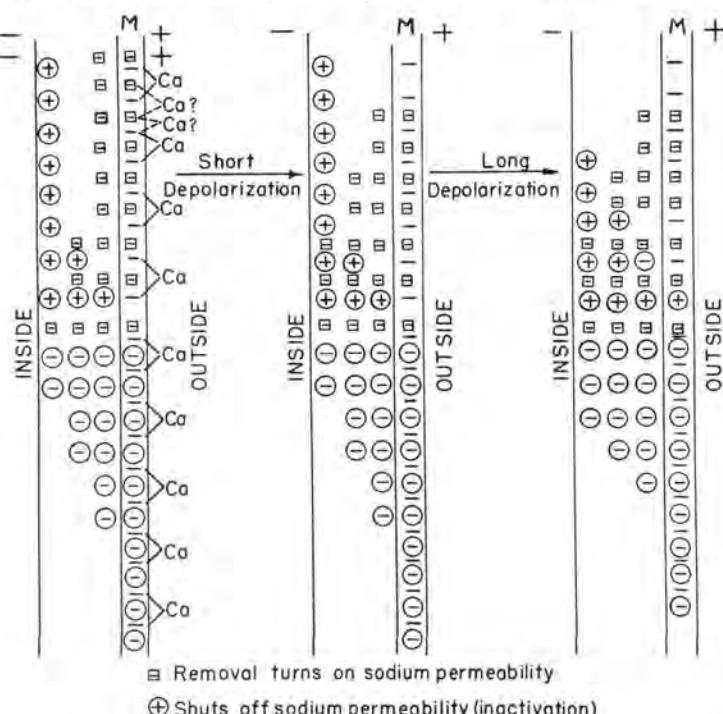
inner boundary, are probably larger and therefore more sluggish; they subsequently drift in the smaller electric field towards the outer boundary and secondarily reduce sodium permeability again in a process called "inactivation."

Dr. Shanes feels that it would be premature to contend that all permeability changes can be ascribed to one principle. He is planning a working model employing these principles to determine to what extent the kinetics of permeability change in living systems can be duplicated. In the meantime, he is exploring the mathematical relationships that may apply.

Underlie All Sensations

Such studies with monomolecular films are useful not only for the help they provide in visualizing the processes occurring in living membranes but, more importantly, for the new experiments they suggest for testing the concepts to which they have led.

Since these permeability changes underlie all sensations, muscle and nerve action, plus certain of the body's metabolic processes, fuller knowledge of their mechanism might eventually find application in an understanding of many disorders such as myotonia and myasthenia gravis and metabolic diseases such as diabetes. One of Dr. Shanes' most recent publications was in *Nature*, Volume 188, Number 4757, (December) 1960.



Dr. Shanes' hypothetical representation of the distribution of lipophilic cations and anions in a resting excitable membrane (first column) and during two successive periods of a moderate depolarization.

ALLERGY

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recorded occurrence of experimental allergic thyroiditis.

Severe damage to the thyroid gland was found at later stages, and has been found as long as six months after immunization. By using the Strain 13 animals and the adjuvant, it was possible to produce the disease in severe form and at very early periods with only a single injection.

Skin tests of the animals revealed delayed hypersensitivity as early as five days after injection, and such hypersensitivity was present in all animals with thyroiditis at seven weeks.

Although antibodies were found in the blood serum of guinea pigs at some stages of the disease, they were far less constant in their appearance and association with the disease than was the delayed hypersensitivity. This close correlation of delayed hypersensitivity and the experimentally induced disease suggests that cellular immunity is more important in allergic thyroiditis than is the presence of antibodies in the blood.

Tissues Transferrable

The experimenters point out that the greatest contribution of inbred, "histocompatible" animals to research on autoimmune diseases is that lymph nodes and other tissues, as well as thyroid and skin, may be transferred from one animal to another with no more immunologic reaction to foreign protein material than if these tissues were being removed from the animal and given back to him.

The experiment, reported at the April meetings of the Federation of American Societies for Experimental Biology in Atlantic City, appears in the current issue of the *Journal of Experimental Medicine*.

Perinatal Studies Show EEG Pattern Trends

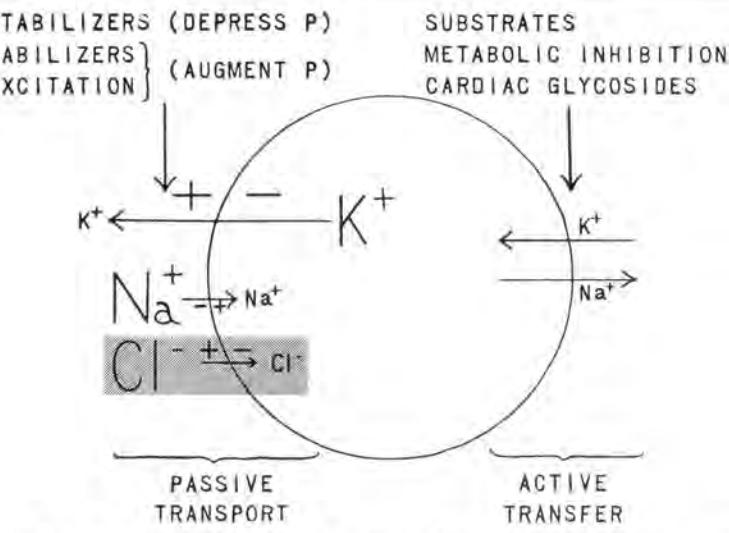
Studies of normal rhesus monkeys at National Institute of Neurological Diseases and Blindness' Laboratory of Perinatal Physiology, Puerto Rico, have added to knowledge of changes in the brain's electrical activity that occur during growth and maturation. In general, patterns of electrical activity (electroencephalograms) in the monkeys followed developmental trends found in other animals and man; that is, the greatest changes occurred shortly after birth but soon became stabilized into the adult forms.

Changes Observed

During the first month of life, the EEG patterns remained similar to those found on the first day of life, but in the second month a marked change in amplitude and rhythm occurred. At one year of age, an adult pattern was seen which continued throughout the 30-month period of observation. Results also showed that differences between wakefulness and sleep patterns could be discerned on the first day of life, i.e., earlier than previously thought.

In addition, maturational changes in sleep patterns occurred earlier and developed more quickly than those of the waking state. About the end of the first week of life, sharp waves or "spikes" bearing a considerable resemblance to epileptic patterns were observed in the drowsy state and are considered to be a normal occurrence.

The study was conducted by Dr. Maria I. Robert de Ramires de Arellano of the NINDB Laboratory of Perinatal Physiology and was reported in *Experimental Neurology*.



A schematic diagram showing a distinction between "passive" ion transfer (i.e., that due solely to concentration and potential differences) and "active" ion transfer (i.e., that against the passive forces brought about by metabolic processes). The conditions affecting these two types of transfer are also shown.

Clue to Hormone Split Of Enzyme Suggested By Common Property

Following is a report on a paper presented at the recent 45th Annual Meeting of the Federation of American Societies for Experimental Biology.

The recently discovered ability of steroid hormones and certain other compounds to split a key mammalian enzyme may lie in characteristics shared by both types of substances. Studies have now indicated that this common property of the compounds is a flat surface devoid of electrical charges.

The scientists had shown earlier that various steroid hormones can alter and thus inhibit the normal reaction of an important enzyme, crystalline glutamic dehydrogenase (GDH), one which is responsible for the chemical buildup or breakdown of the amino acid glutamic acid.

They demonstrated for the first time that a hormone can directly affect the physical structure of an enzyme, in this case by fragmenting GDH into four smaller molecules. This action could determine the direction which the cells' metabolic processes will take—toward energy-giving breakdown or cell-building protein synthesis. Three steroid hormones, all female sex hormones, produced the interference, while cortisone, another hormone tested, did not.

Stems from Finding

The present study stems from the finding, by other scientists, that o-phenanthroline (OP), a potent zinc-finding reagent, also splits GDH and thus it was thought that zinc held the enzymes together. But since the steroid hormones cannot bind zinc and because of the structural similarity between OP and such hormones, Drs. K. Lemone Yielding and Gordon M. Tomkins of the National Institute of Arthritis and Metabolic Diseases wondered whether OP might work by some other mechanism.

The NIAMD scientists have now found that several nonzinc-binding analogs of OP are effective in splitting GDH, indicating that some other property is probably responsible for their ability to alter the structure of the enzyme. This common property appears to be related to the physical form of such enzyme modifiers, that is, they all possess a flat, uncharged surface which may enable these compounds to interfere with the forces which hold the enzyme molecule together. Further studies of how this enzyme is altered by such compounds may lead to a better understanding of the manner in which hormones control enzymes.

Source Book Published On Cardiac Prosthesis

The first source book on Prosthetic Valves for Cardiac Surgery has just been published by the Charles C. Thomas Co. of Springfield, Ill.

Consisting of formal papers and informal discussions presented at a September 1960 conference of heart surgeons in Chicago, the volume is edited by Drs. K. Alvin Merendino, University of Washington; Andrew G. Morrow, Chief of the Surgery Branch, NHI; C. Walton Lillehei, University of Minnesota; and William H. Muller, Jr., University of Virginia.

Sponsored by the Surgery Study Section, DRG, and financed by a grant from the Heart Institute, the conference brought together some 250 participants and guests, representing both active and interested medical workers and research workers in industrial firms manufacturing prosthetic materials.

In planning the conference, the Study Section noted that there are now 51 research groups in the United States either working directly on valve prostheses or doing closely related work, and that recent applications for grants have been indicating a lag in the exchange of information in the field.

ROBBERY

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reservation by way of North Drive.

When they arrived at the rear of the Office Building, Pvt. Van Dusen got out of the police car, and accompanied by Burford and Calhoun, went into the construction office to get the registration card.

As the three men came out of the building with the registration card, Calp, who was standing beside the police car with Pvt. Kaponin, pulled out his gun, slugged Kaponin on the back of the head, and ran around to the other side of the car.

Kaponin, stunned but recovering (the wound required four stitches), whipped out his gun and fired at Calp through a rear window of the car. None of his four shots took effect but the man surrendered.

Meanwhile, Calhoun, witnessing the gunplay, brandished his revolver and started running. Pvt. Van Dusen ordered him to halt and then fired one shot, which struck the fleeing man in the left foot.

Following extensive questioning by the police and FBI agents, called in because the reservation is Federal property, Calp and Calhoun were charged with armed robbery and kidnapping.

They were held without bond pending a preliminary hearing in People's Court in Rockville.

Not the least bizarre feature of the near-tragic episode was the fact that the gunmen delivered the payroll to its intended destination.

Pituitary Control of Fat Transport Affected by Doses of Ethyl Alcohol

Presented at the 45th Annual Meeting of the Federation of American Societies for Experimental Biology, April 1961.

Drs. R. P. Maickel and R. Paoletti of the National Heart Institute's Laboratory of Chemical Pharmacology have found that large single doses of ethyl alcohol interfere with pituitary control over the fat transport system. By some mechanism not yet clarified, the alcohol causes the pituitary to secrete excessive amounts of ACTH. This hormone, in turn, causes the adrenal glands to release other fat-mobilizing hormones. As a result, excessive quantities of triglycerides (neutral fat) are mobilized from the body's adipose tissue. Entering the blood as free fatty acids, this fat is carried by the plasma to the liver, reconverted to triglyceride, and deposited in this organ.

Triglycerides Increase

Previous work in this laboratory had shown that single doses of 4.8 to 6.0 grams of alcohol per kilogram of body weight resulted 18 hours later in a threefold to fivefold increase in liver triglycerides in female rats. These doses were roughly equivalent in humans to about six to ten double martinis (very dry). That these increases were due to fat mobilized from adipose tissue rather than to increased fatty acid synthesis by the liver was shown by the linoleic acid content of the deposited fat.

Since linoleic acid cannot be synthesized by the liver of the rat, all that present must have been of dietary origin. When the deposited fats were analyzed by gas chromatography, their linoleic con-

tent was virtually the same as that of adipose tissues, indicating that this tissue had been their source.

The finding that alcohol did not produce these effects in rats whose pituitaries had been removed suggested that the effects of alcohol on fat transport might be mediated through hormones from this master gland. The most likely suspect was ACTH, which not only stimulates fatty acid mobilization directly, but also triggers the release of other fat-mobilizing hormones from the adrenal glands. Thus further studies explored the response of the pituitary-adrenal system to alcohol.

Secretion Excessive

Evidence of pituitary-adrenal activation began to appear within two hours after the administration to rats of 6.0 gm/kg of alcohol. This activation was manifested by: 1) a fall in adrenal ascorbic acid, accompanied by a sharp rise (150 to 200 percent) in plasma corticosterone; and 2) a 100 percent rise in plasma free fatty acids. In addition, the activity of tryptophan peroxidase (TPO), a liver enzyme whose activity is an indicator of pituitary-adrenal stimulation, increased by 250 percent in six hours. All of these signs indicated that alcohol had evoked excessive secretion of ACTH.

To confirm these observations, the scientists next studied the effects produced in rats by a single large dose of ACTH. This was injected in a gelatinous suspension, so that the ACTH would be released into the blood at a relatively slow rate. The effects were very similar to those of alcohol: a fall in adrenal ascorbic acid, a rise in plasma corticosterone and free fatty acids, and increased TPO activity. The ACTH also caused the deposition of large quantities of triglycerides in the liver.

Stress Effects Similar

It is interesting to note that these effects of alcohol, classified as a depressant, are identical to the effects produced by such "stress" situations as prolonged exposure to cold. They may also play an important role in the development of the liver cirrhosis often found in alcoholics, in which chronic deposition of excessive fat in the liver is believed to lead eventually to severe damage and necrosis. The earlier finding that these effects are prevented by adrenergic blocking agents has stimulated further studies, now underway, to clarify the mechanisms by which alcohol stimulates ACTH hypersecretion and by which these drugs block its harmful effects.

NIH Orchestra to Play Second Annual Concert

The NIH Orchestra will present its Second Annual Concert at 8:30 p.m. on May 16 in the Clinical Center auditorium.

The 45-piece orchestra, sponsored by the Recreation and Welfare Association of NIH and formed in the fall of 1959, includes nurses, scientists, administrators, secretaries, clinicians, and teenagers of NIH families.

The conductor, Mark Ellsworth, concertmaster of the National Gallery Orchestra, considers the concert primarily as a sort of graduation exercise and windup of the season for the players, rather than as an occasion to show off to the public.

There will be no tickets or admission charge for the concert.

Two Mechanisms Control Tissue Uptake of NE

National Heart Institute studies indicate that the uptake of norepinephrine (NE) by brain, heart, and spleen proceeds both by passive diffusion and by a low-capacity concentrating mechanism. When the tissue medium contains little NE, its uptake by these tissues is chiefly by the concentrating mechanism, which probably involves a carrier enzyme and appears to use energy generated by cell metabolism to move NE into the tissues against an opposing concentration gradient. When the medium contains higher concentrations, however, the mechanism becomes saturated, and uptake above this saturation value proceeds by passive diffusion.

Findings Published

These studies were conducted by Drs. H. J. Dengler, H. E. Spiegel, and E. O. Titus, of the NHI Laboratory of Chemical Pharmacology. Their findings were reported in *Science*.

The scientists measured the uptake of norepinephrine labeled with tritium in tissue slices from various parts of the brain and from heart, spleen, liver, adrenal cortex, and muscle. All of these tissues have adrenergic nerves (for which NE is the neurohormone), and brain, heart, spleen, and adrenal cortex contain large quantities of stored norepinephrine.

Concentration Rises

The experiments demonstrated a norepinephrine concentrating mechanism in brain, heart, and spleen tissue. When the incubation medium contained low NE concentrations (5-25 micrograms/ml.), tissue concentrations rose as high as four times that of the medium. When the medium contained higher concentrations, the NE "pump" became saturated. Uptake above this saturation value was by passive diffusion, the tissue NE concentrations increasingly reflecting those of the medium. No concentrating mechanism was evident in tissue from liver, muscle, or, surprisingly, from the adrenal cortex, a major source of circulating NE.

The concentrating mechanism was blocked when reserpine or metabolic inhibitors such as ouabain were added to the medium. This suggested that the mechanism involved active NE transport, using energy derived from cell metabolism to overcome an unfavorable concentration gradient. However, the present studies did not rule out the possibility that the mechanism might involve chemical

Farewell Party Honors Mollie P. Breyere, NCI

Mrs. Mollie P. Breyere, Supervisory Traffic Clerk, NCI, retired May 1 after 21½ years in the Civil Service.

One hundred and fourteen people attended a farewell party in her honor in building T-19 April 27.

Her friends and coworkers presented her with a set of patio furniture and an electric grill for use at the Breyere's summer home on the Severn River near Annapolis.

Mrs. Breyere, a native of Washington, held several government posts prior to 1944 when she first became associated with NIH in the Transportation Audit Office. She joined NCI in October 1947 as a travel clerk.

In 1956 Mrs. Breyere received a Superior Work Performance Award for "broad knowledge of rules and regulations, good judgment . . . and unvarying patience and courtesy."

Mrs. Breyere's husband, Edward, retired in 1951 from the Research Grants Division of NIH. Their son, Dr. Edward J. Breyere, was formerly a research fellow at NCI and is now Associate Professor in the Department of Biology, American University.

Mr. and Mrs. Breyere have lived in Maryland since 1929 and now make their home in Kensington.

Lab Refresher Courses Offered at CD Center

A series of 20 laboratory refresher training courses, varying in length from one to four weeks, will be presented by the Laboratory Branch of the Communicable Diseases Center in Atlanta, Ga., during the period of September 11, 1961, through April 13, 1962.

The courses will deal primarily with laboratory methods in the study and diagnosis of various infectious diseases. In addition, eight unscheduled courses will be given by special arrangement.

Information and application forms may be obtained from the Laboratory Branch, Communicable Diseases Center, U.S. Public Health Service, Atlanta 22, Ga.

binding or adsorption of NE by tissue components.

The scientists noted that the drugs that inhibited the concentrating mechanism also sensitize adrenergic organs to administered NE. Thus the mechanism might play an important role in ending the biological action of NE on these organs by taking it up for delivery to an intracellular storage site. This cellular redistribution would neutralize the action of NE as effectively as would its destruction by monamine oxidase or other enzymes.

Muscle Enzyme Action Site Revealed By Fluorescent Antibody Technique

Following is a report on a paper presented at the recent 45th Annual Meeting of the Federation of American Societies for Experimental Biology.

Research on diseases caused by enzyme defects may be aided by the recent application of the Coons fluorescent antibody technique to locate endogenous enzymes, Drs. E. W. Emmart, S. S. Spicer, W. A. Turner and J. G. Henson, National Institute of Arthritis and Metabolic Diseases, report.

This technique, an immunological binding of antibody to antigen, serves as a precise method of detecting a specific antigen within tissue and localizing a particular enzyme.

It has now been found that this method can also be used to study other endogenous enzymes, that is, enzymes present in and native to the tissue. Heretofore, the method had been used largely to demonstrate exogenous antigens injected or present as a result of infection.

In the present studies glyceraldehyde-3-phosphate dehydrogenase (GAPD), an enzyme important in the intermediate steps in glycogen conversion, has been localized in the mitochondria of the wing and leg muscles of the cockroach. This insect was used because of the large size of its muscle fibers and a high concentration of GAPD in muscles of great metabolic activity.

The antibody method for identi-

fying endogenous enzymes presupposes that the enzyme can be purified and can act as an antigen when injected into experimental animals. In this study, GAPD was isolated from rabbit muscle, purified, and injected into guinea pigs to obtain the anti-GAPD solution (antibody). Serum samples with a high concentration of antibody were combined. The globulin fraction was then removed and coupled to a fluorescent dye.

When the cockroach muscle fibers containing antigen are tagged with fluorescent antibody, the fluorescence appears as a transverse band composed of small mitochondria in the region referred to as the "I band." This localization supports an earlier view that the I band is the seat of chemical energetic processes and glycogen conversion.

It was observed that mitochondria are displaced when the fibers are contracted or expanded, indicating that they are intimately associated with the myofibrils composing the fiber.

This study indicates that GAPD is not specific to a single species, as the enzyme was prepared from rabbit muscle, and suggests that the use of fluorescent antibody to localize enzymes within tissues may be applied to studies of the possible role of specific enzyme defects in certain diseases.

DEDICATION

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Director, will preside at the ceremonies.

The presentation of guests will be made by Dr. John W. Knutson, Chief Dental Officer of the Public Health Service, and the invocation will be delivered by the Rev. William R. Andrew, CC Chaplain.

The building will be formally dedicated by Secretary Abraham A. Ribicoff, who will unveil the name of the Institute, mounted on the stone facade beside the main entrance.

Music for the occasion will be played by the United States Marine Band, conducted by Capt. James King.

The new building is constructed of reinforced concrete with a brick exterior. With an additional two stories below ground, it provides over 42,000 square feet of working space containing the most advanced laboratory and research equipment.

The Norair Engineering Corporation was the contractor for the project, and the architect was Ted Englehardt of Silver Spring.

Guests will be invited to inspect the building following the dedication ceremonies.

New Booklet Describes 2 Causes of Blindness

Cataract and Glaucoma—Hope through Research, a pamphlet describing the two principal causes of blindness in the United States, has been prepared by NINDB and published recently by the Public Health Service.

The importance of early diagnosis of these eye diseases is stressed in the 16-page illustrated brochure. It points out that an estimated one million persons in the United States have glaucoma, and that thousands of them go blind unnecessarily because diagnosis and treatment have been delayed.

The pamphlet also describes the advances that have been made through research at NINDB and other medical centers in this country and abroad in the treatment of this disease and of cataracts.

Single copies of the pamphlet—PHS Publication No. 793, Health Information Series No. 99—may be obtained without charge from the NINDB Information Office. Multiple copies may be obtained from the Superintendent of Documents, U.S. Government Printing Office, Washington 25, D.C., at 15 cents per copy.

CONFERENCE

(Continued from Page 1)

and bringing new findings to rapid application for the welfare of the patient.

It also stressed the need for additional and better trained basic and clinical research scientists; research-oriented physicians; highly-trained specialists in such fields as biostatistics and medical electronics; and paramedical personnel including nurses, rehabilitation workers, physical therapists, home nurses and homemakers. Also emphasized was the need for the continuing education of the physician.

Coding Urged

In the area of scientific communication, the report urged accurate, high-speed methods of coding and retrieving medical data and consideration of a central recording facility for patients' life-time health records. It also recommended further international exchange of scientific information and personnel, and the support of collaborative studies between investigators in many countries.

Both public and private agencies should, according to the report, make better and fuller use of the media of mass communication to educate the public.

"We wholeheartedly believe," the report states, "that we are at the beginning of a biomedical revolution whose triumphs against disease and human suffering can only be dimly seen at the present time."

To Be Distributed

The report will be printed and made available for wide distribution in the near future.

Chairman of the conference, which represented 22 of the country's leading scientists and physicians in the heart and cancer fields, was Boisfeuillet Jones, Special Assistant for Health and Medical Affairs, DHEW.

Participants included Drs. E. Cowles Andrus, H. Stanley Bennett, Julius H. Comroe, Jr., Michael E. DeBakey, Harold S. Diehl, Kenneth M. Endicott, Sidney Farber, J. R. Heller, Charles Huggins, Irvine H. Page, I. S. Ravdin, Peyton Rous, Harold P. Rusch, Howard E. Skipper, H. Burr Steinbach, George E. Wakerlin, James Watt, Myron E. Wegman, Paul Dudley White, Robert W. Wilkins, J. Walter Wilson and Irving S. Wright.

Ribicoff Attends

DHEW Secretary Ribicoff, PHS Surgeon General Terry, and NIH Director Shannon also attended the White House meeting.

The conference staff was headed by Dr. Margaret H. Sloan, Special Assistant to the Director, NCI, and Lealon E. Martin, Staff Assistant for Scientific and Public Information, NHI.

Change-About Lab Modules Demonstrate Methods of Improved Space Utilization

Two mockup laboratories demonstrating a new concept in space utilization are open for inspection in the Division of Research Services.

The key to the new design is the 5 x 10 ft. module, a basic building unit which may be used in a variety of flexible combinations that readily yield to modification as research needs change. The system enables the investigator to tailor space in accordance with his needs.

The larger of the two demonstration laboratories is 15 x 20 ft., and the smaller is 10 x 20 ft.

The wider laboratory is recommended for investigators who need ample space for the use of island equipment. The smaller laboratory is planned as a combined work-and-study area that does not require the placement of equipment between wall benches.

Two of the smaller laboratories could be combined to utilize a full peninsular bench.

An office cubicle measuring 5 x 10 ft. is set up next to the smaller laboratory to demonstrate how privacy can be achieved by partitioning an area only one module wide. The equivalent space could also be used for the storage of records, or to house sterilizers, centrifuges, and similar bulky equipment.

Three types of 2"-thick partitions with good fire and sound resistance are exhibited.

Gas, water, air, vacuum, and other utility lines have been in-

stalled horizontally above the ceilings and along the inside of the exterior wall of the mockup rooms to demonstrate how utilities can be hung between floors.

Utility lines can be dropped through a vertical chase at any multiple of five feet and extended horizontally along the walls.

A special raceway with outlet valves has been devised to provide added flexibility.

As yet, no laboratory buildings at NIH employ the 5-ft. modular width. The newest (the Biologics Standards Building and the Dental Building) are designed on the basis of a 12½-ft. modular width, and the laboratories, offices, and animal rooms in these buildings are constructed in multiples of 12½ ft.

The mockup rooms are still in the experimental stage and are part of a continuing search for design improvements in laboratory construction. They were opened in April in Building 11, following a study of laboratory space utilization at NIH and recommendations that led to the mockup construction.

The entire project is the work of the newly created Development Section of the Research Facilities Planning Branch.

Scientists and technicians desiring to inspect the laboratories may arrange to do so by calling Ext. 4996. Administrative officers and others who plan and equip laboratories at NIH are also invited to join any of the scheduled tours.



The design of future NIH laboratories may be strongly influenced by reactions to a mockup area recently opened for the inspection of research investigators. Among the first to visit the area are (left to right) Dr. Robert H. Felix, NIMH Director, and Richard L. Seggel, NIH Executive Officer, accompanied by Chris A. Hansen, DRS Chief. Their guide is John A. Cofrancesco, Acting Chief of the Development Section, Research Facilities Planning Branch, DRS, who planned the project and directed its construction.

Flieger, NCI, Promoted

Kenneth H. Flieger, a member of the Cancer Institute's Office of Information and Publications since

1957, was appointed an Assistant Information Officer of NCI, effective April 16, with responsibility for supervision of its Information and Education, and Reference and Distribution Sections

2 Fellowship Programs Established in DRG

The Research Fellowships Review Branch, DRG, has announced the establishment of two new fellowship grant programs, Career Research Professor and Special Fellowship, and the revision of a third, Senior Fellowship.

The Career Research Professor Grant Program has been established to support individuals of demonstrated capacity to pursue with distinction a professorial career in independent research and training.

Grants are awarded initially for five years of support and are renewable at five-year intervals. In this first year the award will be made only to schools of medicine, osteopathy, dentistry, and public health. The earliest effective beginning date is July 1, 1961.

Purposes Outlined

The Special Fellowship Grant Program will provide support for promising young investigators who are not yet eligible for a higher level but are considered by the applicant institution to be an important addition to its teaching and research staff.

This grant program is in addition to the present Special Fellowship awarded directly to individuals for advanced or special training.

The Senior Fellowship Grant Program, formerly limited to pre-clinical science departments, has been expanded to include clinical departments and certain departments in university graduate schools and other institutions.

This program is for the support of individuals with at least five years of relevant research experience beyond the doctorate, who have demonstrated high potential for a research or academic career.

Bacteriologists' Society Changes Its Name

The Society of American Bacteriologists, one of the oldest biological societies in the United States, has changed its name after 61 years of existence, according to a recent announcement.

The organization has been renamed the American Society for Microbiology. The new name is considered more descriptive of the broadened scope of the Society's membership and interests.

Founded in 1899, the Society has grown to a membership of over 6,500. In addition to holding an annual meeting for scientific interchange, it produces four scientific publications—*Journal of Bacteriology*, *Bacteriological Reviews*, *Applied Microbiology*, and *Bacteriological Proceedings*—and a news magazine.

Cholinesterase Activity Localized in Cultured Skeletal Muscle Cells

Studies of living muscle cells grown in tissue culture without nerve tissue show that cholinesterase, an enzyme important in neuromuscular transmission, initially is located throughout the cell, rather than at the end-plate region of the nerve-muscle junction as in innervated muscle cells. No cholinesterase-containing end-plates were found in the cultured cells, but in the more mature stages the enzyme was located along certain cross-striated bands (Z-lines) which traverse the muscle fibers.

Conducts Impulses

Cholinesterase is the enzyme which regulates neuromuscular transmission by destroying acetylcholine, a chemical necessary for the conduction of impulses across synapses and across the nerve-muscle junction. The localization of cholinesterase activity in skeletal muscle cells may lead to a better understanding of the mechanisms responsible for impulse transmission from nerve to muscle and possibly, from the end-plate region to other parts of the muscle fiber. Sites of activity of the enzyme have been determined in living cells of chick embryo skeletal muscle by Dr. W. K. Engel, Medical Neurology Branch, National Institute of Neurological Diseases and Blindness and results published in the *Journal of Histochemistry and Cytochemistry*.

Since there is no direct method for the cytochemical localization of a specific cholinesterase, the enzyme was detected by its action on substrates introduced into the cells and by its susceptibility to various inhibitors. Under these circumstances, the enzyme demonstrated had properties like the specific cholinesterase known to be of physiological importance in muscle activity.

Diffusely Located

Cultured muscle cells in three stages of development showed sites of cholinesterase activity as small brown granules located diffusely in the cytoplasm and clustered in the regions around the cell nuclei. However, no enzyme activity was found in the cell membrane surrounding the muscle fiber or within the nuclei. The finding that no motor end-plates were formed by the muscle cells suggests that nerve tissue is essential for the development of end-plate structures. It also appears that before innervation cholinesterase activity is widely distributed throughout the cell. Subsequent to innervation, enzyme activity is increased at the motor end-plates and repressed elsewhere.

VISITORS POSTED IN DBS LOBBY



Visiting scientists from abroad are greeted on their arrival at the Division of Biologics Standards by finding their names posted in the lobby of the DBS building. The announcement board, recently installed, serves a dual purpose—to inform the staff of the visitor's presence and to welcome the visitor. Dr. Yasuyuki Egashira, of Japan's Ministry of Health, is pictured inspecting the board, which carried his name and identification during a recent visit.

Helen Anderson Leaves For Position in BSS

Helen M. Anderson, Assistant Administrative Officer, NIDR, and an NIH employee since 1949, transferred recently to the Division of Air Pollution, Bureau of State Services, PHS, as Administrative Officer.

Miss Anderson rose rapidly from clerk to Fellowships Assistant in the Research Fellowships Branch, DRG, and in 1953 became Administrative Assistant in the Scientific Reports Branch, DRS. In 1958 she transferred to her recent position in NIDR.

Miss Anderson was President of the NIH Recreation and Welfare Association last year.

The demonstration of cholinesterase along the transverse striations known as Z-lines raises an additional consideration: that is, whether or not a mechanism involving cholinesterase and acetylcholine may be active along the Z-lines to conduct the activating impulse into the center of the skeletal muscle cell and thus activate the muscle fiber. Previous physiological studies by other investigators indicate that incompletely innervated muscle cells and denervated adult muscle show, in regard to sensitivity to applied acetylcholine, a similar diffuse pattern along the muscle fibers. Thus, support is added to the suggestion that under certain conditions an acetylcholine-cholinesterase mechanism may function at sites of the muscle fiber other than the motor end-plate.

Applications for Grants Increase 39% Over '60

The Division of Research Grants has announced the receipt of 39 percent more research grant applications between January 20 and March 1, a total of 27 working days, than during the same period last year.

Three thousand, one hundred and twenty-three grant applications were logged in by DRG between these dates compared to 2,250 in 1960. From these figures, the Division estimates that 3,600 requests for support of research projects will be reviewed by the National Advisory Councils meeting in June.

The amount of support requested totals more than \$90 million, not including applications for funds made available under the new "Center Grants" program.

DBS Issues Pamphlet On Rh Factor in Blood

A new pamphlet, *Blood and the Rh Factor*, has been issued recently by the Division of Biologics Standards.

The 8-page publication describes in simple terms the composition of human blood, the differences in blood groups, and the significance of the Rh factor, especially in relation to the new-born child.

Single copies of the pamphlet, PHS Publication 790, may be obtained from the DBS Information Office, and multiple copies may be ordered from the U.S. Government Printing Office, Washington 25, D.C., at 10c each or \$7.50 per hundred.

Influenza Bibliography Is Now Available

A new publication, *An Annotated Bibliography of Influenza*, was issued recently by the American Institute of Biological Sciences, supported by a grant from NIAID.

The work, Volume I of a continuing bibliography on influenza, is designed to fill the need for a unified and up-to-date reference source on influenza research.

The current publication contains 176 references covering the period June 1 through September 30, 1960, extracted from approximately 2,600 U. S. and foreign journals.

A second volume, to be published soon, will give references over the period January 1, 1957 through May 31, 1960.

Influenza research in 1960 will be covered by quarterly supplements to the first two volumes, including in the fourth-quarter publication an index for the entire year.

The bibliography may be obtained from the American Institute of Biological Sciences, 2000 P Street, N. W., Washington 6, D. C.

CC Pamphlet Outlines Referral Procedures

The Clinical Center is now distributing the latest edition of its booklet, *Current Clinical Studies and Patient Referral Procedures*.

Issued primarily for physicians in private practice and those associated with hospitals and clinics, this 38-page publication contains up-to-date information concerning patient referral procedures, eligibility requirements, brief description of the clinical studies currently in progress, and types of patients required for participation in research studies of all seven Institutes.

Copies of this pocket-size booklet, PHS Publication No. 284, are mailed regularly to interested medical, scientific, and related professional people requesting it, as new editions are published.

The Clinical Center also issues a leaflet for the lay public which explains how CC patients are selected and how to apply for admission as a study patient. It is titled *Patient Admission Procedures*, PHS Publication No. 500.

Requests for both publications should be addressed to the CC Information Office.

4-Nation Trip Scheduled For Dr. Robert T. Hill

Dr. Robert T. Hill, Deputy Chief of the Special Programs Review Branch, DRG, left Bethesda May 7 for London, first stop on a six-week trip as NIH representative at scientific meetings in Great Britain, Israel, Australia, and Japan.