

the

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TV Techniques To be Tested in PHS Orientation

A closed-circuit color telecast entitled "An Experiment in Education-Communication," will be transmitted live by WNIH-TV, the Clinical Center System, to the North Building auditorium of DHEW beginning at 1:30 p.m., on April 19.

This program, featuring selected portions of the NIH segment of the PHS Senior Level Orientation Program, is designed to test the feasibility and effectiveness of this presentation technique.

Dr. R. C. Arnold, Assistant Surgeon General for Personnel and Training, PHS, and Dr. Murray C. Brown, Chief, Clinical and Professional Education, CC, will moderate the program, presented in two parts.

The first part will consist of closed-session discussions on "Pro-

(See TV TECHNIQUES, Page 8)

New NIH Sound-Color Film To Be Seen Here Thursday

The new NIH sound-color motion picture, produced for public information use, will have its first public showing Thursday, April 14, in the CC auditorium.



Dr. James M. Stengle, of DRG, who as "Dr. Robertson" is chief narrator of the new NIH motion picture, examines a print of the film in his office.

Beginning at 11 a.m., the 16 mm. film, which has a running time of 24 minutes, will be presented at half-hour intervals. The last of this series of five screenings is scheduled to start promptly at 1 p.m.

The picture is being shown here for NIH employees prior to its availability for distribution and for internal use. It has also been cleared for television and will be one more addition to NIH information media.

Titled simply "The National Institutes of Health," the film was produced by Potomac Film Producers with the cooperation of the Department of Agriculture Motion Picture Service and NIH information personnel.

The Washington commercial firm
(See NIH FILM, Page 7)

Dr. Homer Smith To Deliver Next NIH Lecture

Dr. Homer W. Smith of the New York University College of Medicine, recognized as one of the outstanding leaders in the field of renal physiology, has accepted Dr. Shannon's invitation to deliver the next in the series of NIH lectures.

The lecture, illustrated by slides, will be presented in the CC auditorium on Tuesday, April 26, at

8:15 p.m. NIH employees and their guests are invited to attend.

Dr. Smith reports that the lecture, titled "From Fish to Philosopher," will be largely a condensation of his book by that name. It will



Dr. Smith

deal with the broader perspectives of paleontology and the evolution of the vertebrates, with emphasis on the regulation of the internal environment.

It will also include an interpretation of the advanced evolution of consciousness in the vertebrates, a discussion of recent studies of sodium secretion in the nasal glands of birds and reptiles, and the osmotic concentrating operation of the mammalian kidney.

A graduate of the University of Denver and Johns Hopkins University, Dr. Smith is Professor of Physiology and Director of the Physiological Laboratories at the New York University College of Medicine. He has been the recipient of two Guggenheim Fellowships, in 1928 and 1930.

Under the 1928 Fellowship, Dr. Smith conducted field studies of the lungfish in Central Africa. From information collected there, he published not only technical papers but his first book, a novel entitled *Kamongo, or the Lungfish and the Padre*, which became a Book-of-the-Month-Club selection.

Dr. Smith has also published several technical books on renal physiology, as well as many scientific papers.

FOUR AID ELEVATOR-STALLED NURSE; CARRY BLOOD 10 FLOORS

By Mary Henley

When a county-wide power failure enveloped NIH temporarily on Tuesday morning, March 29, four CC building engineers averted a possible crisis by coming to the rescue of a CC Blood Bank nurse who was trapped in an immobilized elevator.

Mrs. Peggy Wirdzek, a new nurse in the Blood Bank, was taking an emergency blood cart to the 10th floor operating room when her elevator was stalled in total darkness between floors by the power failure.

Although soon released from the elevator, Mrs. Wirdzek faced the problem of getting the heavy supply of blood to doctors waiting 10 floors above with an anesthetized patient prepared for surgery.

John Bartgis, Donald Urban, Robert Williams, and John Carpenter, all of the Plant Engineering Branch, DRS, solved the dilemma. They appeared on the scene with flashlights, transferred the blood containers from the cart to trays

obtained from the CC kitchen, and escorted Mrs. Wirdzek up the 10 flights of stairs to deliver the valuable cargo to the operating room.

This prompt and thoughtful action is recognized by Dr. Allan Kliman, Supervisor of the CC Blood Bank, and others in the Laboratory of Blood and Blood Products, DBS, as typical of the quiet way in which the building engineers volunteer their services.

Mrs. Wanda S. Chappell, Head Nurse of the Blood Bank, echoes this opinion, adding that the men's interest in this area is reflected in prompt responses to appeals for blood whenever an emergency need for donors arises.

Facilities Need Studied

The NIH Disaster Control Group is now studying the need for improved emergency standby facilities and is preparing more explicit instructions for the guidance of all employees in the event of future emergencies.



Nurse Peggy Wirdzek and the four building engineers who helped her carry a heavy supply of blood to the 10th floor of the Clinical Center during a recent power failure, reenact the scene for NIH Photographer Jerry Hecht and the NIH Record. The engineers, clockwise from left, are John Bartgis, Donald Urban, John Carpenter, and Robert Williams.

the Record

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NEWS from PERSONNEL

Federal Service Entrance Exam

This examination provides opportunities for careers in a wide variety of positions throughout the Federal government. The examination will be given on May 14. Applications must be filed by April 28. This is the last opportunity for taking the examination until late this year. Additional information and application forms are available in the Recruitment and Placement Section, Bldg. 1, Rm. 21.

Health Benefits Information

The leaflet "For You and Your Family," which summarizes the Health Benefits Program in general terms, has been sent to the Institutes and Divisions for distribution among employees.

Increased Rates for Shortage Category

The Civil Service Commission has taken action to increase the minimum starting rate for the following NIH positions at grades GS-5 and GS-7: chemists, physicists, mathematicians, mathematical statisticians, architects, and professional engineers.

The new basic rate of compensation for the positions listed above is \$4,940 for GS-5 and \$5,880 for GS-7. The new rates will become effective May 1.

It was found that the Federal Government starting salary in these categories was, at grade 5, about \$1,500 below industry, and at grade 7 about \$570 lower than the rate offered by industry to the superior graduate. It is expected that these adjustments will attract qualified people in these vital fields.

Evaluation Standards

NIH employees are reminded that Position Classification Standards are available for review in

NIH Brochure Revised, Now in Distribution

Distribution of the newly revised edition of "The NIH Brochure," which for many years has been one of the most widely used NIH information publications, was begun last week.

The new edition, revised by the Office of Research Information with the cooperation of the Institute and Division Information Offices, reflects the advances made in research knowledge and techniques within the past few years.

It also explains, by text and chart, the organizational structure of NIH and describes, in general terms, the functions of NIH components and the types of research activities conducted here.

The 28-page booklet is liberally illustrated and contains a map showing building locations and uses. Its green and white cover consists of a recent aerial photograph of the NIH reservation.

The brochure is widely distributed, not only internally but to outside organizations and individuals interested in knowing what NIH is and does. It is also given to NIH visitors by the Special Events Section, CC.

the office of the Personnel Assistants serving their areas. These standards are published by the Civil Service Commission and are used by the Personnel Management Branch for purposes of evaluating job titles, series, and grades. Application of these standards is mandatory.

Before any new standard is published, it is circulated to Government agencies for study and critical comment. New and revised standards adopted by the Commission are reviewed by the Personnel Management Branch, thus assuring current knowledge of changes and the effect of change on NIH positions.

'Cherokee' Captain Inspects Radiation Safety Program

Comdr. John F. Thompson, captain of the U.S. Coast Guard cutter *Cherokee*, which for 10 years has carried NIH radio-active waste to sea for disposal, was here for conferences and inspection of the NIH Radiation Safety Program on March 23.

Accompanied by George P. Morse, Chief, Plant Safety Branch; Dr. Howard L. Andrews, Radiation Safety Officer, PSB; and Joseph M. Brown, Jr., Chief Health

Physicist, Radiation Safety Office, PSB, Comdr. Thompson visited the NIH Isotope Laboratory (Bldg. 21), where he witnessed a demonstration of the methods employed here in preparing radio-active waste for disposal.

Comdr. Thompson also conferred with other NIH officials, including Dr. Joseph E. Smadel, NIH Associate Director for Intramural Research, and Dr. G. Burroughs Mider, Associate Director in Charge of Research, NCI.

Mr. Morse explained that the NIH radio-active waste is sealed in 1,500-lb. concrete burial vaults for delivery to the *Cherokee* at Norfolk by NIH trucks. Three to five trucks, he said, travel in convoy under the direction of Radiation Safety Office personnel who accompany them in an NIH car, with radiation monitoring equipment.

At various stages of the operation, the trucks and NIH personnel, and subsequently the Coast Guard cutter and its crew, are carefully monitored.

The burial vaults are transported to sea by the *Cherokee* and dumped approximately 100 nautical miles due east of Norfolk, where the depth is over 6,500 feet.

Mr. Morse estimates that the gross weight of NIH waste and containers disposed of during the past year amounted to 72 tons.

Report Shows NIH Lag In Health Campaign

The PHS report of March 31, only two weeks before the end of the Federal Service Campaign for National Health Agencies and Joint Crusade, revealed NIH still in last place with 37.7 percent employee participation.

The report showed the Bureau of State Services on top with 69.7 percent, followed by the Office of the Surgeon General with 66.6 percent, and the Bureau of Medical Services with 44.9 percent participation.

Percentage of participation by Institutes and Divisions follows:

DGMS	90.7
NIDR	75.9
NIAMD	71.6
DRG	63.2
DBS	63.2
DRS	58.2
NIAID	49.5
NCI	40.2
OD-OAM	36.3
NIMH	26.0
NHI	20.1
NINDB	16.8
CC	9.5



A concrete vault containing radio-active waste is inspected by Comdr. John F. Thompson, captain of the Coast Guard cutter *Cherokee*, which carries NIH waste to sea. With Comdr. Thompson are (left) Dr. Howard L. Andrews, Radiation Safety Officer, PSB, and Joseph M. Brown, Jr., Chief Health Physicist, Radiation Safety Office, PSB.

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.

Tumor Studies Can Benefit From Virology Techniques

Excerpts from introductory address by Dr. Joseph E. Smadel, Associate Director for Intramural Research, National Institutes of Health, at the Symposium on Phenomena of the Tumor Viruses held under the sponsorship of the Virology and Rickettsiology Study Section, Division of Research Grants.

During the past few years, there has been developing a ferment of interest in viruses and human neoplasms. There are many reasons for the current activity. Some of these are the following: Tissue culture techniques have opened a wider vista for sighting hitherto unrecognized viruses than did the previous expansions of the horizon which accompanied the introduction of the suckling mouse, the embryonated egg and the ordinary laboratory mouse into common isolation procedures. Morphologic techniques as exemplified by electron microscopy of thin sections have been given tantalizing results with human tumors while immunofluorescent microscopy and the more recent ferritin antibody procedures for use in electron microscopy seem to provide potent weapons for studies on viruses and cancer. Immunologic procedures have become more delicately sensitive. The scientific world has been stimulated by the infectivity of naked viral nucleic acids. Smallpox and measles, in which infection is almost invariably associated with a typical full-blown clinical and pathological picture, are no longer regarded as the prototypes of most viral diseases. Instead, poliomyelitis, with its high incidence of inapparent infections and rare paralytic manifestations, is considered typical of a large number of viral diseases. Moreover, salivary gland and adenoviruses have joined the group exemplified by herpes virus and other microbial agents which persist for long periods of time in clinically recovered persons.

Translation of Findings

Translation of such findings to the virus-cancer problem provides support for two ideas, namely, (a) tumor development may occur in only a small proportion of people who are infected with the hypothetical inciting virus and (b) the causal agent may persist in the individual for years, eliciting its carcinogenic effect long after initial infection. Another development which has stimulated virologists

is the findings with the polyoma agent. These demonstrated, more dramatically than earlier observation with chicken malignancies, that multiple types of tumors may arise as a result of infection with a single virus. Can we hope for a simplification in man such as this in mice and chickens?

Virologists Study Cancer

While virologists have been persuaded to join the exploration of the viral etiology of human cancers primarily because of one or another of the scientific developments just mentioned, there were other factors which assisted in their conversion. A number of investigators were concerned, during and immediately after World War II and the Korean War, with virologic diseases of importance in foreign lands to Americans stationed there and to the indigenous peoples. Others were engaged in work which culminated in the successful control measures for poliomyelitis. Many such persons were willing to rededicate their efforts to another difficult and important cause, i.e., cancer. Fortunately, the interest of the lay public, reflected through the action of Congress, has made funds available for support of research in this field.

Diagnostic Virology Discussed

Like most of you here, I view the problem of the viral etiology of human cancer with hope and enthusiasm. Moreover, I have confidence that investigators entering this field will attain the success here they have had in their research on the classical viral infections of man.

Although my assigned task was to present briefly certain of the background information which has excited the interest of virologists, particularly, in working on the problem of the viral etiology of human cancer, I cannot refrain from discussing a subject which has provided a central theme for

my own work for many years, namely, diagnostic virology. . . .

The basis of diagnostic virology is to be found in Koch's postulates as revised by Rivers in 1937. The latter's ideas, restated somewhat in the light of experience with a host of subsequently recognized viruses, are essentially as follows: A virus is presumed to be of etiologic significance in a given human disease if (1) the agent is present in the tissues or excretions of most persons in the acute stage of the illness and is absent or infrequently present in normal persons or patients with other diseases, and (2) patients who yield the virus during their acute illness develop with regularity, during convalescence, specific antibodies against the agent. Virologists have practically abandoned the idea that Koch's final postulate, i.e., reproducing the disease in a normal host, must be fulfilled in man if a virus is presumed to be a human pathogen. However an increasing number of the viruses which have been shown by the criteria of Rivers to be of etiologic importance in non-fatal human disease have been inoculated into human beings. Sometimes such transmission studies have resulted in the reproduction of the classical manifestation of the original disease, viz., dengue, measles, and trachoma. In other instances the experimental disease has occasionally mimicked the original but more frequently has reproduced only part of the clinical picture, viz., lymphocytic choriomeningitis and adenovirus infections. Finally, some laboratory strains of viruses, notably the attenuated polioviruses, induce only subclinical infection.

Caution Urged

One would hope that a thorough application of old, new and yet to be developed isolation techniques would yield viral agents from human cancers with which one might fulfill Rivers' criteria. Encouragement will certainly be given to those who try such approaches. However, along with encouragement should go a word of caution since these approaches will undoubtedly yield numerous agents which will be unrelated etiologically to human cancer, even though they may have been present in the patient and not indigenous to the systems employed for the isolation work. The persistent efforts over the years to propagate in the laboratory the viruses of hepatitis and of epidemic hemorrhagic fever provide documentation of the frequency with which agents may be recovered that are not of etiologic significance in the diseases under study. Application of the serologic diagnostic criteria mentioned above revealed the irrelevancy of the extraneous iso-

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Autoimmunity Concept Studied

The concept of autoimmunity has become popular within recent years to explain the occurrence of certain diseases whose etiology is still unknown. According to this concept, it is possible for an individual to become sensitive to substances normally present in body cells and tissues, and to produce antibodies against these substances. The resultant antigen-antibody reactions in the tissues are thought to lead to the pathological changes noted in the disease.

This concept has been useful in explanations of Hashimoto's disease of the thyroid gland. Individuals with this disorder were found to have circulating antibodies in their serum which reacted with their own thyroglobulin. Presumably, the antibodies were reacting with the thyroglobulin in the thyroid gland and causing the tissue damage characteristic of the disease.

As a result of this work, many studies were begun by various investigators to re-examine other diseases of unknown etiology, in an attempt to discover if they might also be expressions of autoimmunity.

At the present time rheumatoid arthritis is being considered as such a disease by many investigators, partly because the "rheumatoid factor" which is present in the serum of rheumatoid arthritis has many of the properties of an antibody.

In a related disease, systemic lupus erythematosus, it has been found that the serum contains a whole family of antibodies, some against normal cell nuclei, some against cytoplasm, and others against sub-components of both nuclei and cytoplasm.

With these findings in mind, Dr. Joseph J. Bunim and his associates at the National Institute of Arthritis and Metabolic Diseases made a comprehensive serological study of patients with Sjogren's Syndrome to determine what antibodies might be present in their serum.

This syndrome is characterized by hypofunctioning of both the tear and salivary glands and is often accompanied by rheumatoid arthritis. Any two components of the ocular-salivary-arthritis triad are sufficient to establish the diagnosis. Aside from the occurrence of the arthritis, the syndrome is of particular interest because the pathological changes found in both the tear and salivary glands are strikingly similar to those seen in the thyroid glands of persons with Hashimoto's disease.

(See AUTOIMMUNITY, Page 6)

New Technique Describes Venous Circulation in Eye

The application of an intricate radiographical technique to intact living eyes has enabled a National Institute of Neurological Diseases and Blindness investigator to describe for the first time the complex intraocular venous circulation of the cat eye. Little known anatomical details and theories of circulation, which may be applicable to human eyes, have been clarified by the use of this technique.

Although radiographic methods have been used to study the vascular system of the living brain, the valuable tool previously had not been applied successfully to the vessels within the eye. Known as intraocular venography, the new technique is of potential value in diagnosing some eye disorders and in studying such conditions as congestive glaucoma, in which vascular disturbances occur. The study, by Dr. Bruce E. Cohan of the NINDB Ophthalmology Branch, was reported in the current *A.M.A. Archives of Ophthalmology*.

Vein Perfused

In performing the experiments, the anterior ciliary vein of the cat was exposed, divided, and cannulated with a needle attached to tubing and a syringe. The vein was then perfused with a radiopaque material and film packets were placed flat in a space provided by the removal of the cat's nasal orbital wall. During perfusion, exposures were made by appropriate positioning of a central X-ray beam.

An interpretation of these radiographs enabled Dr. Cohan to design a schematic composite of the circulation pattern and to describe little known details of the intraocular venous system. Since other comparative studies have shown that the intraocular circulation of the cat and dog resembles that of man, Dr. Cohan suggests that the findings of this study may be valid for the human eye.

Radiopaque Material Seen

Radiographic evidence failed to confirm the presence of previously described swellings and constrictions in the veins of the choroid, a vascular layer between the sclera and the retina. It is possible, however, that the elevated venous pressure during the experimental procedure obscures such caliber changes which might be present under physiologic conditions. In addition,

high-speed perfusion resulted in the appearance of radiopaque material in the anterior aqueous chamber—between the cornea and the iris—implying a connection between the chamber and the intrascleral veins. The intrascleral veins were also found to communicate with the veins of the ciliary body, which connects with the iris.

Intraocular Pressure Elevated

The study showed that when perfusion rates were increased, intraocular pressure also increased substantially. In several experiments, air was not completely flushed from the tubing and harmless amounts were introduced into the circulation. The finding that large amounts of air were trapped in the vortex sinus when intraocular pressure was elevated suggested that outflow from the vortex vein had been impeded. According to Dr. Cohan, this tends to confirm the many speculations that venous outflow is strangled under conditions of elevated intraocular pressure.

Deformities Found After Fetal Anoxia

The effects of temporary anoxia upon fetal mortality, and upon the frequency of congenital abnormalities, including cleft palate, were studied by Miss Lee Feild, Dr. S. J. Kreshover, and J. E. Lieberman, National Institute of Dental Research. Initially, the onset of gestation was established in 249 Sprague-Dawley rats between 2 and 3 months of age.

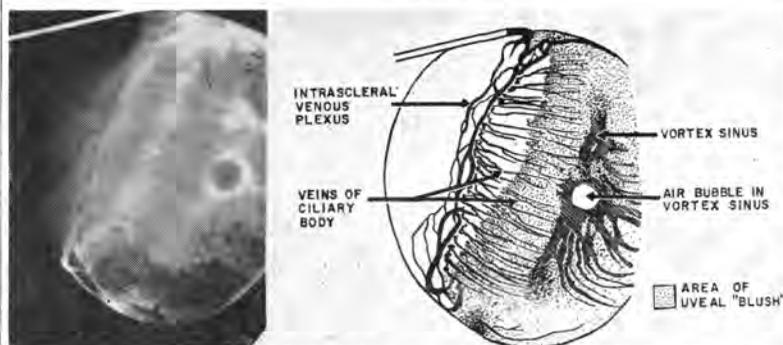
At periods of gestation ranging from 9 to 17 days, the animals were anesthetized and both uterine horns were exposed through abdominal incision. The circulation to either the right or left uterine horn was occluded by clamping the vascular supply, and the uterus was then returned to the body cavity. (This technique provided both experimental and control fetuses within the same parent animal.)

After the scheduled period of circulatory arrest, ranging from 10 to 60 minutes, the clamps were removed. The uterus was again returned to the body cavity, and the incision was then sutured. One day before expected term delivery, the young were extracted by cesarean section and examined.

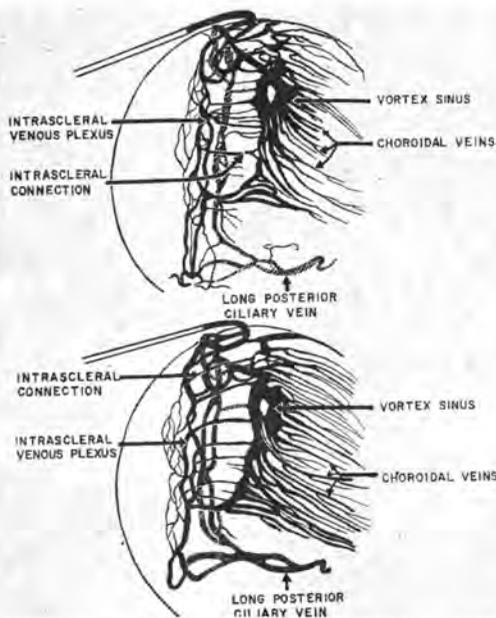
Results showed that developmental anomalies occurred only in fetuses of the 169 rats treated between the 12th and 15th days of gestation. Twenty-six of the 507 viable experimental young in this group were deformed, whereas 2 of the 523 viable control young were deformed.

The greatest frequency of deformities (17.6%) occurred after a 45 minute vascular occlusion on the 15th day. There were 13 in-

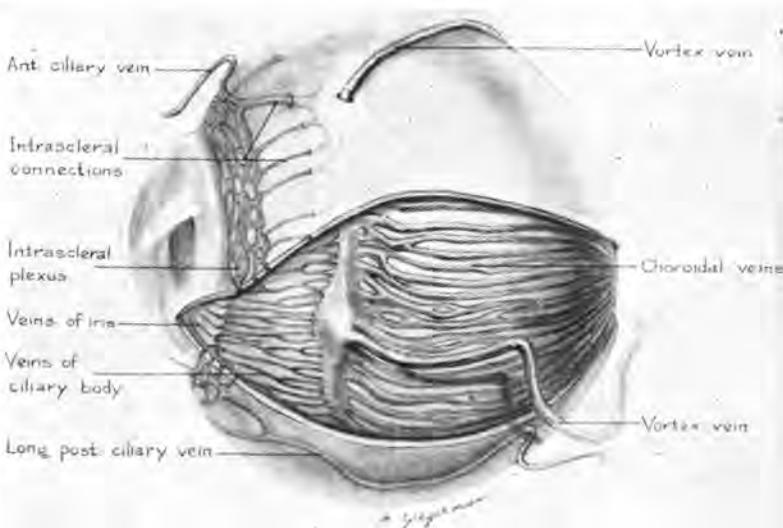
(See ANOXIA, Page 6)



Oblique projection obtained during pump infusion at approximately 4 cu. cm. per minute; air was also injected. It demonstrates intense filling of the intraocular venous systems and trapping of an air bubble in a vortex sinus.



Top—Beginning uveal filling: Increase in the infusion rate to approximately 2 cu. cm. per minute. Bottom—Moderate uveal filling: Increase in the infusion rate to approximately 4 cu. cm. per minute.



Schematic composite of the radiographic anatomy of the intraocular venous circulation of the cat. The sclera is drawn as if it were semi-transparent in order to demonstrate the veins within it and the location of the vortex sinus in the underlying uveal system. A strip of sclera has been removed to reveal the pattern of the uveal venous circulation.

Aminoaciduria and Dwarfism Are Studied in Familial Syndrome

A familial syndrome characterized by aminoaciduria, dwarfism and muscular underdevelopment has been investigated through detailed metabolic and genetic studies reported by Drs. Leon E. Rosenberg, Donald M. Watkin and Peter S. Mueller of the National Cancer Institute at the 24th Annual Meeting of the American Institute of Nutrition. Clinical features of the syndrome were originally described by Drs. Peter T. Rowley, Watkin, Mueller and Rosenberg. Aminoaciduria is a term indicating the presence of abnormally large quantities in the urine of free amino acids, the building blocks from which proteins are constructed.

In the studies now reported, the *propositus*, a technical term for the original person presenting a disorder who serves as the basis for a genetic study, was a 12 year old boy exhibiting all the above mentioned features of the disorder. A brother and sister, also with growth retardation, died at ages 7 and 8 respectively. Two living brothers, aged 20 and 6, have aminoaciduria without other stigmata, while both parents are totally unaffected.

The *propositus* developed normally until one-and-a-half years of age when his rate of linear growth and weight gain decreased markedly. His weight at the time of these studies were in the third percentile for his age (*i.e.*, 97% of all boys of the same age are taller and heavier). He demonstrated no cataracts, enlargement of his liver or spleen or signs of rickets and has shown on repeated examinations normal liver and kidney function and normal overall carbohydrate, calcium phosphorus metabolism.

Disturbances Ruled Out

These negative observations have led the authors to rule out many known disturbances involving amino acid metabolism such as galactosemia (the presence of high concentrations of galactose, a sugar derived from milk, in the blood), Wilson's disease (a disorder of copper and amino acid metabolism accompanied by cirrhosis of the liver and the degeneration of the lenticular nuclei of the brain), Lowe's syndrome (a familial abnormality consisting of multiple renal tubular defects, aminoaciduria, growth failure and cataracts), "H" disease (a familial disorder characterized by neurological disturbances and the excretion of indoles and amino acids), rickets (a disease of ossification of bone usually due to vitamin D deficiency or disturbed kidney function), scurvy (a disease resulting from vitamin C deficiency), poisoning by heavy metals (such as lead, mercury and cadmium), and the Fanconi syndrome (a disorder characterized by rickets and disordered glucose, amino acid, calcium and phosphorus metabolism).

The *propositus* and his brothers excrete daily in their urine from

5 to 20 times normal quantities of the amino acids. Quantitative determinations of individual amino acids in urine, using the column chromatographic technique of Spackman, Stein and Moore of the Rockefeller Institute, showed 15-20 fold increases in the excretion of the amino acids serine and threonine and less striking excesses of lysine, histidine, alanine and tyrosine. Similar determinations on blood plasma revealed concentrations of amino acids which were normal or depressed. These studies together with specific renal clearance tests of kidney function suggested that the aminoaciduria was due to defective absorption in the tubules of the kidney.

Protein Synthesis Studied

The presence of growth failure in the *propositus* and two siblings and its absence despite aminoaciduria in another two led the authors to investigate protein synthesis in the *propositus* by the metabolic balance study technique, (*i.e.*, the careful measurement of the differences between intake and output of certain nutrients and calories which leads to an expression of the retention or loss of protein or other body constituents). On a weighed diet containing 4 g. protein per kg. body weight per day (3 to 4 times normal intake) and 100 calories per kg. body weight per day (2 to 3 times normal intake), the *propositus* stored protein and gained about 50 g. weight per day. In a subsequent study of a similar diet, the addition of 1 g. threonine and 0.5 glycine as daily supplements to the dietary regime induced small increases in protein storage. In the most recent study on a diet containing 2.5 g. protein per kg. and 100 calories per kg. body weight per day supplemented by threonine and lysine, the withdrawal of first lysine and then threonine did not change weight gain or protein retention. The threonine supplementation, however, was associated with a marked increase in the urinary excretion of uric acid, by-product of the synthesis of certain types of nucleoprotein.

Genealogical Survey Made

A genealogical survey of the family of the *propositus* revealed

Drug Metabolism Sped by Drug Pretreatment

Pretreating rats with a variety of drugs has been found to increase the activity of drug-metabolizing enzyme systems in the liver, thus decreasing the duration of drug action on the body, report National Heart Institute scientists.

The findings were presented at the meeting of the Federation of American Societies for Experimental Biology by Drs. A. H. Conney, I. A. Michaelson, and J. J. Burns of the NHI's Laboratory of Chemical Pharmacology. This laboratory is conducting a broad program of basic studies aimed at elucidating the factors regulating duration of drug action. Previous studies in this laboratory had shown that special enzyme systems in liver microsomes, tiny particles in liver cells, inactivate many drugs as well as other compounds foreign to the body by converting them into compounds which the kidney can excrete.

Enzyme Activity Tested

In the currently reported studies, Dr. Conney and co-workers investigated the ability of microsomal enzyme systems in rat livers to metabolize several commonly used drugs following repeated doses of the same or another drug. Rats were pretreated for four days and their livers incubated with test drugs to determine microsomal enzyme activity. The scientists also tested enzyme activity in live, pretreated rats by measuring the duration of action of test drugs. Drugs used in the study included barbiturates, muscle relaxing drugs, analgesics, anti-rheumatic agents, a carcinogenic hydrocarbon, and an antihistamine.

Results of the liver incubation studies showed that pretreatment with phenobarbital, barbital, phe-

nylbutazone, orphanedrine, or aminopyrine caused "several-fold increases" in the ability of liver microsomes to metabolize hexobarbital, zoxazolamine, phenylbutazone, and aminopyrine, report the investigators. They obtained evidence of accelerated drug metabolism in living, pretreated rats by demonstrating a shortened duration of action of hexobarbital, zoxazolamine, meprobamate, and carisoprodol in animals that had received repeated doses of these drugs.

Enzyme System Stimulated

In other *in vitro* studies, the investigators observed that pretreatment with the hydrocarbon, 3,4-benzopyrene, stimulated the microsomal enzyme system that metabolizes zoxazolamine, but not the hexobarbital-metabolizing system. "In accord with this, 3,4-benzopyrene administration shortens the duration of zoxazolamine paralysis from 730 minutes to 17 minutes but does not shorten the duration of hexobarbital hypnosis," they report. Interestingly, the duration of action of both zoxazolamine and hexobarbital was shortened in rats pretreated with the antihistaminic drug, chlorcyclizine.

Importance Seen

"The findings that pretreatment of animals with one drug can speed up the metabolism of the same or another drug may be of considerable importance when evaluating the pharmacological activity of drugs that are given repeatedly, either alone or in combination," stated the Heart Institute scientists.

VIROLOGY

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no other members of the family with combined growth disturbances and aminoaciduria. However, in addition to the two brothers previously mentioned, a maternal uncle, a maternal aunt and a double cousin were found to have aminoaciduria. To the geneticist, these findings suggest an autosomal dominant trait with incomplete penetrance and variable expressivity, probably transmitted through the maternal side of the family.

Understanding of this unusual syndrome is for the moment incomplete. Unquestionably a renal tubular defect resulting in aminoaciduria is present, but the nature of the metabolic defect preventing growth in the *propositus* remains obscure. The analogy to the problems of the patient harboring a cancer which robs the body of amino acids is obvious and challenging.

lates; in brief, either the patients develop no antibody against the isolate or if antibodies were present they did not increase in titer during the disease.

If the near future fails to provide techniques by which a viral agent presumably causing human cancer can be put through the standard procedures to fulfill the diagnostic criteria demanded as proof of etiology, then we might decide *a priori* what data would partially satisfy the basic demands of diagnostic virology . . .

Whatever temporary compromise is chosen, whatever data are decided on as satisfying, at least partially, the principles of diagnostic virology, one must remember, as Rivers pointed out, the importance of tempering ingenuity of compromise with the "priceless attributes of common sense, proper training, and sound reasoning."

Hormone-Like Effects Produced by Menthol

Menthol, the substance that gives peppermint its characteristic odor, has been found to have an effect similar to that of the female sex hormone progesterone on the metabolism of galactose. This discovery indicates that menthol may be another rare example of a non-steroidal compound that produces some of the same physiological effects as a hormone. The finding was reported by Drs. T. D. Elder, S. Segal, E. S. Maxwell, and Y. J. Topper, of the National Institute of Arthritis and Metabolic Diseases, at the meeting of the Federation of American Societies for Experimental Biology.

Menthol's hormone-like effect became apparent during studies of galactosemia, a relatively rare hereditary disorder of children. Infants with this disease are unable to tolerate galactose, a sugar present in milk, since they lack one of the enzymes necessary for galactose metabolism. If milk is allowed to remain in their diet, it quickly creates a toxic condition leading to mental retardation, cataract formation, liver damage and early death. The basic nature of the disease was discovered in 1955 by scientists at the National Institute of Arthritis and Metabolic Diseases, who first made the biochemical "diagnosis" and pinpointed the exact enzyme that was deficient.

Further studies of the disease led to the discovery that injections of the hormone progesterone enabled galactosemic children to metabolize at least some galactose. Apparently the hormone enables the body to overcome the enzymatic block. This finding was reported to the Federation meetings last year and set an important precedent for research on other metabolic disorders caused by enzyme deficiencies.

The hormone-like activity of menthol was discovered by accident during detailed *in vitro* studies of progesterone's effect on galactose metabolism. Menthol was being employed to study some of the reactions when it was noted that the compound had the same ability to stimulate galactose metabolism as progesterone. Oral doses of menthol were then tried in two galactosemic children and enabled them to metabolize the same amount of galactose as they would have with progesterone injections.

The therapeutic implications of these findings have yet to be explored since only tracer doses of galactose have been used in the clinical trials. Also, the mechanism by which either progesterone or menthol exert their effects *in vivo* is not yet known. Menthol may prove to be of particular value in

Link Found Between Metabolism And Transport of Electrolytes

Recent work at the National Heart Institute has explored the metabolic processes which provide energy for the "ion pump," whereby the cell can actively and selectively transport ionic substances (electrolytes) across the cell membrane against opposing electrochemical forces. Dr. Joseph Hoffman of the NIH Laboratory of Kidney and Electrolyte Metabolism has found that adenosine triphosphate (ATP), a high-energy compound which energizes muscular contraction and many other energy-consuming biological processes, also drives the ion pump.

Previous work on intact red blood cells by Dr. E. T. Dunham, formerly of the same laboratory, had indicated that ATP might be the fuel for the ion pump. In studies following this lead, Dr. Hoffman used red cell "ghosts"—cells from which the normal contents had been removed by hemolysis. These ghosts provided a "cleaner" system to study than the intact cell because the ghosts, while retaining the membrane permeability characteristics of the intact cell, could be reconstituted incorporating only known substances, including phosphorylated intermediates normally incapable of penetrating the membrane of the intact cell. The metabolism of the incorporated substances could then be observed without interference that might result from the other metabolites and metabolic processes of the intact cell. The studies revealed that ATP was the specific energy source for the ion pump; however, if no ATP was incorporated into the ghosts, the pump would still work (though less efficiently) if substances that would generate ATP were incorporated.

Active, selective transport of ions across the cell membrane by the ion pump is the most important factor in the maintenance of proper electrolyte balance within the cell. The pump uses energy generated by cell metabolism to offset the passive loss of ions across the cell membrane by osmosis or ion exchange diffusion. The ion pump, therefore, is essential to the regulation of cell volume and to the maintenance of the differences between the intracellular and extracellular fluids both in kinds and in concentrations of electrolytes. Presumably because one ion cannot replace the

further studies of this phenomenon since the menthol molecule is a much smaller and simpler one than that of progesterone.

metabolic functions of another, the proper concentrations of the proper ions must be maintained in the body's different fluid compartments. This would be impossible but for the delicate balance struck between passive loss on the one hand and active transport on the other.

ATP, the fuel for the ion pump, is the essential product of both glycolysis and oxidative phosphorylation, the processes whereby the energy generated by the oxidation of fats or carbohydrates is stored in this compound's high-energy phosphate bonds. The basis of the ATP molecule is the purine adenine, which can add the carbohydrate ribose to form adenosine, then phosphate ions to form adenosine diphosphate (ADP) and ATP respectively. In these reactions a considerable portion of the energy liberated by oxidation is conserved as chemical potential; this energy is then released when ATP is catabolized.

Essential Feature Found

Although other substances that would generate ATP would also drive the pump, Dr. Hoffman found that the essential feature was the presence of an adenine-based substance. Thus adenosine would drive the pump because it could be phosphorylated in the cell to ATP. Other substances could activate the pump in the presence of ADP by providing the phosphate groups to convert it to ATP. That ATP was the specific fuel for the pump was also indicated by the finding that iodoacetate and arsenate, which inhibit the production of ATP from glycolysis, nevertheless did not affect the pump when incorporated ATP was used as substrate. However, when glucose and the enzyme hexokinase were incorporated along with ATP, the pump was inhibited because the ATP would be used up in the phosphorylation of glucose, leaving none for the pump to catabolize.

The above results suggest that, to use ATP, the ion pump requires the presence of an enzyme, an ATPase. Such an enzyme has been isolated from red blood cells by Dr. R. P. Post of Vanderbilt University and appears to possess the same activation characteristics as does active ion transport in the red cell ghost. The evidence is therefore strong that this enzyme either is the ion pump or else is an intimate component of an ion pump complex.

Because it is one of the most important means by which the kidney maintains its careful control over the body's electrolyte, acid-base, and water balance and by

AUTOIMMUNITY

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The NIAMD serological study showed that an abnormally active immunological response was present in patients with Sjogren's Syndrome. Almost all the patients gave positive responses to the bentonite flocculation test and sensitized sheep cell agglutination test for rheumatoid arthritis, even though only 8 patients out of 21 had definite clinical signs of the disease.

The majority of patients were also found to have a serum constituent that had a specific affinity for cell nuclei, and in this respect they resembled patients with systemic lupus erythematosus. Another interesting finding was the presence of an antibody to human thyroglobulin (14% of the cases) which was similar to the one found in Hashimoto's disease.

Dr. Bunim reported, in the Stoneburner Lecture at the Medical College of Virginia, that these findings demonstrate that Sjogren's Syndrome patients exhibit much greater immunological reactivity than those with rheumatoid arthritis alone, and the diversity of the humoral antibodies may indicate a basic derangement of antibody production.

This NIAMD research thus provides further support for the developing concept of autoimmunity, and indicates that immune mechanisms may be playing an important part in the pathogenesis of these diseases.

ANOXIA

(Continued from Page 4)

stances of palatal clefts, 8 of which occurred in the progeny subjected to anoxia on the 14th day. In addition, there were 18 experimental young with limb defects or other abnormalities, five of which also had cleft palates.

Data on fetus mortality showed that a high incidence of death was also related to circulatory interference, particularly after occlusion on the 13th gestational day, and after the longer periods of circulatory arrest.

The findings were reported at the meeting of the International Association for Dental Research.

which the individual cells of the body maintain homeostasis, active ion transport affects to some degree virtually all of the body's metabolic processes. Thus a fuller knowledge of its mechanism might eventually find application not only against cardiovascular-renal disorders but against many other diseases as well.

Dr. Hoffman reported his findings at the meeting of the Federation of American Societies for Experimental Biology.

NIH FILM

(Continued from Page 1)

wrote the script and supervised production. The U.S.D.A. Motion Picture Service was responsible for direction and for camera and technical services, and NIH provided a variety of liaison and technical assistance.

This involved script editing, arranging for the use of locations and "props," provision of electrical services, scheduling of scene shooting, and the participation of NIH personnel who appear in the film in their own right or as actors.

Hamsters Provide Actors

Many of the actors were recruited through cooperation of the Hamsters, the R&W-sponsored NIH dramatic group. In the pre-cut version approximately 200 NIH employees appeared. This number was reduced to about 40 in the final edited version.

Principal narrator of the film is Dr. James M. Stengle, Executive Secretary of the Hematology Study Section, DRG, who takes the part of "Dr. Robertson," an NIH biochemist.

In this role he welcomes a group of NIH visitors and talks to them informally in a conference room setting, explaining the mission of NIH and its origin and development as the main research center of the PHS, now largest in the Nation.

For an explanation of the organizational structure of NIH, its relation to PHS and DHEW, and its use of congressional appropriations for intramural and extramural research and supporting services, "Dr. Robertson" turns the narration over to a professional who plays the part of an NIH administrator, making use of a number of charts.

Shows Research Activities

The film then centers upon activities in the laboratories and shops of NIH, providing a cross section of the kind of research that is done here and the environment that has been created to make such research productive.

This is accomplished by the device of showing the NIH visitors a film of these multiple activities, permitting them to see in a relatively short time many of the vitally interesting operations and procedures that would otherwise require days of actual inspection.

This portion of the film—ostensibly a picture within the picture—is narrated by the voice of a second professional who remains unseen.

In conclusion the narration reverts to "Dr. Robertson," who expresses the point of view of the medical investigator in the never-ending war against disease. He cites major achievements illustra-

Ingenious Drinking Fountain Makes Hit with Quadrupeds



Anita, a kennel-dweller in the NIH Animal Hospital, takes a long cool drink from one of the new hanging water fountains now in use there.

By Betty Mok

Thirsty canine and feline residents of the NIH Animal Hospital may now casually step up to a water fountain for a satisfying mouthful or a long drink, just like any human.

The hanging fountain, a new idea for the animal world, was designed by Dr. William I. Gay, Chief of the Animal Hospital Section, DRS, and John L. Carter, animal husbandryman. Production assistance came from other areas of DRS.

Dissatisfied with the way the conventional shoe box-shaped, stainless steel water pans were constantly being upset or soiled by the animals, Dr. Gay developed a set of standards for a hanging fountain: It should provide a constant supply of fresh water, prevent the water from being siphoned back into the water-supply system, protect the valve from being licked or otherwise soiled by the animals, and permit easy cleaning of the fountain and surrounding area.

With the assistance of the Plumbing Shop, PEB, Dr. Gay and Mr. Carter modified a commercial valve assembly which is activated when the water level in the dish drops, raising a spring against the valve tip and opening it.

Suggestions from the Sanitary Engineering Branch brought about

the addition of a metal cap to protect the valve, and the Metal Shop, PEB, constructed the cap and the special bracket to hold the water bowl. The bowl itself is standard equipment in the animal colony.

Dr. Gay reports that the fountain has proved efficient, labor-saving, and inexpensive to construct and maintain. Eighty are in use in the animal buildings now, and the same model will be used throughout the appropriate quarters on the NIH animal farm. Moreover, the present dog and cat population indicate approval of the innovation.

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TV Council Meeting Open to NIH Staff

Dr. Murray C. Brown, Chief, Clinical and Professional Education, CC, invites interested NIH staff members to attend the spring meeting of the Council on Medical Television, on April 20.

As reported in the March 15 issue of the RECORD, the theme of the meeting will be "Pedagogic Technics in Television."

Registration will be held at 8:30 a.m., April 20, in the CC lobby. Further information may be obtained by calling Dr. Brown, Ext. 2427.

NIH Scientists Attend Federation Meetings, Report Research

Dr. Joseph E. Smadel, NIH Associate Director for Intramural Research, will present one of the more than 120 reports to be read by NIH scientists at the 44th annual meeting of the Federation of American Societies for Experimental Biology, to be held in Chicago April 11 to 15.

Approximately 12,000 experimental biologists from the U.S. and 30 foreign countries are expected to attend the meeting, at which 2,654 scientific reports will be presented by 5,142 authors.

Among those from NIH presenting their research findings will be 12 foreign scientists who are in the U.S. under the NIH International Postdoctoral Research Fellowships Program.

Latest Findings Reported

Findings reported at the meeting will represent the latest information in such fields as fats in coronary disease, radiation and recovery, cancer, organ transplants, nutrition, and drugs affecting human behavior.

The Federation, of which more than 30 members have been Nobel Prize winners, consists of the American Physiological Society, the American Society of Biological Chemists, the American Society for Pharmacology and Experimental Therapeutics, the American Society for Experimental Pathology, the American Institute of Nutrition, and the American Association of Immunologists.

Two New Pamphlets Published by NIMH

Two new information pamphlets were issued recently by NIMH.

Highlights of Progress in Mental Health Research, PHS Publication No. 736, is a selection from studies made by NIMH scientists and grantees during 1959. It tells of the expansion of existing areas of research and of the development of an integrated biological, psychological, and sociological approach to the problems of mental illness.

National Institute of Mental Health, PHS Publication No. 20, is a revision of an earlier edition. It describes the organization and operation of NIMH, with emphasis on the research functions of that Institute in the search for the causes and cure of mental illness.

Single copies of these pamphlets may be obtained without charge from the NIMH Information Office.

Two NIH Doctors Receive Awards From DHEW

Two NIH administrators received awards for meritorious service at the DHEW ninth annual Honor Awards Ceremony April 12 in the HEW Departmental auditorium.

Dr. G. Burroughs Mider, Associate Director in Charge of Research, NCI, received the Department's top honor, the Distinguished Service Award, and Dr. J. Franklin Yeager, Chief, Grants and Training Branch, NHI, received the Superior Service Award.

Dr. Mider was cited for "distinguished service in developing and administering an intramural research program of exceptional excellence in the National Cancer Institute." He also received a gold medal.

Dr. Yeager was honored for his "distinguished service in the program of Federally supported research into the 'cause, prevention, and methods of diagnosis and treatment of diseases of the heart and circulation.'"



Dr. Mider



Dr. Yeager

Dr. Mider was Professor of Cancer Research at the University of Rochester School of Medicine and Dentistry. In that capacity he also served as special consultant to NCI.

An employee of NHI since 1948, Dr. Yeager joined the Grants and Training Branch in 1949, and became its chief in 1951. He was formerly with the Department of Agriculture.

Mrs. Luke Wilson Dies

Mrs. Luke I. Wilson, who with her late husband gave to the U.S. Government the original 92 acres of the NIH reservation, died Thursday morning at the Washington Hospital Center. Story and pictures will appear in the next issue.

7,000 Study Youth Needs At White House Conference

By Bruce Berman

Meeting under DHEW guidance, the sixth White House Conference on Children and Youth brought to Washington on March 27 more than 7,000 delegates for six days of discussion, debate, and stock-taking on needs of children and youth.

Similar White House conferences concerned with the Nation's children and youth have been held every 10 years during this century.

Much of what is now regarded as important for the full development of young people has been shaped by these conferences. Each conference seeks to provide guidance for planning ahead and preparing today's youth for life in the next decade.

The first such conference, called in 1909 by President Theodore Roosevelt, gave impetus to the establishment of the U.S. Children's Bureau in 1912, the enactment of child-labor laws, and organization of the Child Welfare League of America.

In 1919, President Woodrow Wilson's conference established national responsibility in setting minimum health and welfare standards for mothers and children.

What is probably the most comprehensive collection of data on the health and welfare of children ever assembled was a product of the 1930 conference called by President Hoover. In 1950, the mid-century conference developed machinery for continuing activity during the years between conferences.

Invitations to the 1960 Golden Anniversary conference were issued by President Eisenhower on recommendation of the President's 92-member National Committee, made up of leaders in education, health, social work, recreation, re-

ligion, and other areas related to children and youth.

Conference participants included nominees of state committees and national organizations, 500 citizens of other nations, and many public officials.

In the words of DHEW Secretary Arthur S. Flemming, this was a citizens' conference designed "to truly reflect the desires and aspirations of the American people for the children and youth of this country."

Groundwork for the conference was laid by millions of people throughout the country working with private and public agencies at local, state, and national levels.

Each problem presented to the conference was treated from many viewpoints simultaneously and in relation to all segments of the community.

In their consideration of these problems the participants employed a two-pronged approach which (1) examined environmental influences upon young people in a reference frame of "The World Around the Young" and (2) surveyed the current scene from a personal and individual standpoint: "The Young in the World."

Russian Translation And Foreign Grants Transfer to DGMS

Administrative responsibility for the Russian Scientific Translation Program and the Foreign Grants and Awards Section of NIH has been transferred from the Division of Research Grants to the Division of General Medical Sciences under Dr. G. Halsey Hunt.

The Translation Program, directed by Dr. Samuel S. Herman, administers the translation of Russian biomedical literature and makes it available to American scientific audiences.

The Foreign Grants and Awards Section, headed by Dr. Ronald E. Scantlebury, administers the International Fellowships Program and the Visiting Program.

These programs support post-doctoral research training for scientists from other nations, permitting the investigators to carry out a year's training at an outstanding medical research center in the United States. The Fellows are invited to visit NIH during the tenure of the Fellowships.

The Translation Program will have its offices in Room 314, Perpetual Building, Wisconsin Ave., and the Foreign Grants and Awards Section will remain on the reservation, in Building T-18, Room 112B.

TV TECHNIQUES

(Continued from Page 1)

gram Physiology and How Programs Are Born," by NIH Institute Directors. The second part, beginning at 3 p.m., will center around "Research at the Bench and in the Clinic," with scientific presentations focused on "Studies of the Normal," "Mechanisms of Disease," and "The Search for a Cure."

Personnel from various Government agencies interested in the potential uses of television will be invited to view this portion of the program and to participate in the general discussion period at 4:15.

Dr. Murray Brown, who directs the activities of WNIH-TV, expressed appreciation to Eidophor Inc., for technological assistance and for providing the large-screen color projection system.



Three Sections of the Statistics and Analysis Branch, DRG, numbering 56 employees, moved in late March to new quarters in this recently constructed National Bank Building on Arlington Road, Bethesda, at the intersection of Bradley Boulevard. Occupying the second and third floors, the Sections are Statistical Design and Analysis, Statistical Processing, and Research Information. Shuttle bus service is provided from the NIH reservation four times daily. Additional space in the building will be leased by NIH following completion of the second phase of construction, probably this summer.