the NIH Record

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

Vol. XII, No. 25
December 6, 1960

PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

Dr. Leon Heppel To Deliver 10th NIH Lecture

Dr. Leon A. Heppel, Chief of the Laboratory of Biochemistry, NIAMD, and internationally known for his contributions to the science of enzymology, has been selected to deliver the Tenth NIH Lecture. It will be presented at 8:15 p.m., Wednesday, December 14, in the CC auditorium.

Dr. Heppel

Dr. Heppel will speak on "An Enzymatic Approach to Nucleic Acid Chemistry." He will discuss the intricacies of painstaking investigation into the functions and structures of the nucleic acids—deoxyribonucleic acid (DNA) and ribonucleic acid (RNA).

Particular emphasis will be placed upon his use of enzymes such as spleen phosphodiesterase, pancreatic ribonuclease, venom phosphodiesterase, pork liver nuclease, and *Staphylococcus aureus* nuclease, in conducting structural studies of the RNA backbone.

Control Heredity

"The nucleic acids," according to Dr. Heppel, "are the basis of heredity, and control not only the hereditary characteristics of the two million or more different species, but are responsible for individual variances or interspecies differences as well."

He pointed out that "Our greater understanding of nucleic acids will increase our insight into normal growth patterns, hereditary diseases, and may provide new methods of treating and preventing disease."

A former associate of Dr. Arthur Kornberg, winner of the 1959 Nobel Prize in medicine, Dr. Heppel commenced his studies in nucleic acid chemistry in 1947.

Since that time, his work has won for him a Guggenheim Fellowship in 1953 and the Hillebrand Award of the Washington Chemical Society in 1960.

Annual Meeting of R&W To Be Held Tomorrow

The 1960 annual meeting of the NIH Recreation & Welfare Association will be held tomorrow (Wednesday) at 12 o'clock noon in Wilson Hall.

All R&W members are urged to be present to elect officers for the coming year and to hear the annual reports.

Dr. Burney Announces Top Level Changes in Grants Administration

Dr. Ernest M. Allen, Chief of the Division of Research Grants and NIH Associate Director for Research Grants, has been given full-time responsibility as Associate Director, according to an announcement November 30 by Surgeon General Burney.

Succeeding Dr. Allen as Chief of the Division is Dr. Dale R. Lindsay, former DRG Assistant Chief. He will be assisted by Dr. Clinton C. Powell, formerly DRG Assistant Grants Branch Chief for Clinical

Drs. Allen, Lindsay and Powell

Research, who has been named Deputy Chief of the Division.

The reassignments, recommended by Dr. Shannon, are the result of the rapid growth and complexities of NIH research grant activities.

A Commissioned Officer in the Public Health Service, Dr. Allen has been associated with NIH since 1946, first as Assistant Chief of DRG, and from 1951 until his present appointment, as Chief of the Division.

Before coming to NIH has was with the PHS Division of Venereal Diseases.

Dr. Lindsay has been a PHS

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First World Symposium On Health Institutes Meets in Italy Dec. 12

Dr. James A. Shannon, NIH Director, will participate in the First International Symposium on National Health Institutes, to be held in Rome, Italy, December 12-14.

Sponsored by WHO, the Italian Ministry of Health, and the Italian National Health Institute, the Symposium will be an international assemblage of national health institute directors.

Dr. Shannon

Reports and discussions will cover the organization of national health institutes; their functions in scientific research and the safeguard of public health; government controls; and the active participation of the institutes in such problems as field research on infectious diseases, the use of pesticides and psychotropic drugs, air

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New Agreement Spurs Research In the Americas

An agreement designed to foster and coordinate medical research activities in the countries of the Americas was announced jointly last week by the Pan American Health Organization (PAHO) and the United States Public Health Service.

The agreement, concluded by Drs. Leroy E. Burney, PHS Surgeon General, and Abraham Horwitz, Director of the Pan American Sanitary Bureau, focused on three primary points: (1) staff collaboration between the two organizations, (2) development of the PAHO research activities, and (3) definition of forms of USPHS aid that might be applied to PAHO research activities.

The Pan American Health Organization, according to the announcement, will provide moderate financial support to research projects and programs, conduct re-

(See AGREEMENT, Page 2)

350 Invited to Car Pool Conference; Decision on Bus Routes Is Awaited

Three hundred and fifty NIH employees who have indicated a desire to join car pools were invited to attend a meeting scheduled for 1 p.m. last Thursday in the CC auditorium.

All of those invited to the meeting had signified their interest by filling in and returning 3 x 5-inch cards distributed by Plant Safety Branch, requesting home addresses and phone numbers and NIH phone extensions.

Seating arrangements at the meeting were planned so as to bring together, for direct exchange of information, those living in the same communities or along routes between those areas and the reservation.

NIH employees located in office buildings in Silver Spring and Bethesda, who also revealed their interest in car pool membership by returning the inquiry cards, have been supplied by PSB with the home addresses and phone numbers of others in their home areas, to enable them to make contact.

Meanwhile, Plant Safety Branch was awaiting the decision of D. C. Transit System concerning establishment of direct commutation bus service with stops throughout the reservation.

The bus company had been supplied with information obtained from a traffic survey conducted by PSB, indicating that approximately 2,000 NIH employees were interested in the possibility of such service. This was followed recently by a tour of the reservation by company officials to determine possible routes and stops.

The traffic survey was conducted at the request of NIH Management as the first step in an attempt to reduce mounting traffic and parking congestion here.

the NIH Record

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

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'PERSONNEL' TO PERSON

ALL PHS Commissioned Officers have been invited to attend a meeting at 3:30 p.m. today (Tuesday) in the 14th floor auditorium of the Clinical Center.

Mrs. Nora S. Levsky, Field Representative of the Social Security Administration, District Office, will present a motion picture and speak briefly on what the Social Security Act means to the PHS Officer and his dependents. She will discuss recent amendments to the Act and answer questions.

An additional question-and-answer period, beginning about 4:15 p.m., will be devoted to questions on subjects such as Pay and Deductions, Promotion Policy, Insurance (Auto and Life), Survivor Benefits, Medical Care for Dependents, Income Tax Exemptions, C.O. Organizations, and Professional Education Within and Outside the Service.

Also on hand to answer questions will be Dr. William L. Ross, Medical Director, OSG-Personnel; and Mrs. Catherine M. Gardiner, C.O. Unit, NIH.

* * * *

A small group of NIH Civil Service employees with three or more years service who do not have career or career conditional status may be eligible to receive such status under the provisions of a recent Executive Order (E.O. 10880).

This order applies to persons who were serving under unlimited temporary appointments on June 7, 1960 and who had completed two years of continuous service immediately prior to that date. Those who meet these requirements must also be found eligible in a suitable Civil Service Examination.

The PMB is now reviewing its records to determine which employees will benefit from the Executive Order. Those who are found eligible will be notified at the appropriate time.

Questions concerning the provisions of E.O. 10880 should be directed to your Personnel Representative.

AGREEMENT

(Continued from Page 1)

search by its own staff, provide coordination for research projects involving more than one country, and aid in the development of scientists, scientific communication, and other medical research activities.

The U. S. Public Health service, under the agreement, will provide technical advice on research design. In addition, PHS will consider research grant proposals from investigators who may wish to participate in research programs coordinated by PAHO and applications for support to PAHO for research conducted or coordinated by PAHO staff.

Continuing responsibility within the PHS for development of program plans and specific details will be delegated by the Surgeon General to the Office of International Research Activities at NIH.

SYMPOSIUM

(Continued from Page 1)

and water pollution, and control of radio-activity.

Dr. Shannon will serve as chairman of the general session of the Symposium on December 12 and will present a paper on the administration of NIH. He will describe particularly the extra-mural programs, discussing the categorical approach to research, and will emphasize the necessity for developing resources for the future through expansion of manpower and research facilities and broader support of educational institutions.

Dr. Shannon will also participate in a panel discussion on operating research and public health problems, and will describe disease control techniques used in the NIH research program.

Editor Ed, a Veteran at 13, Comes Up the Hard Way

By Ken Stabler

Three years ago come Christmas, Ed Tabor's parents, Drs. Herbert and Celia W. Tabor of NIAMD, presented him with an ingenious rubber-stamp and ink-pad outfit designed for printing.

On a recent visit to the NIH Record office, Ed Tabor, youthful editor of the Station Tribune, and members of the Record staff examine a prior issue of the Record (Nov. 8) which carried Ed's by-line story of the recent NIH children's benefit fair. Record staff, left to right: Mary-Helen Emmons, writer; Ken Stabler, editor; and Betty Mok, associate editor.

By selecting individual letters from the font of rubber type and inserting them in slots provided in the rubber stamp, Ed could spell out words and sentences, four lines at a time.

Once the four lines of type were set, he inked the stamp on the pad and registered the readable impression on paper. And in the process, which he was quick to use, Ed became at once a typesetter and printer.

But there appeared to be no demand for these services, so Ed decided to supply it. That's when he hit upon the idea of putting out a newspaper. In taking this second step he took on the additional tasks of reporter, editor, and publisher.

Publishes First Issue

The result was the first issue of the *Station Tribune*, a rather minuscule paper confined to items of news about children of the reservation and their parents.

Editor Ed at that time was 10 years old, and his laboriously printed paper enjoyed a circulation of five copies, at 1c per copy.

Today, at 13, Ed is still editing and printing the monthly *Station Tribune*, a considerably expanded and improved newspaper with a guaranteed circulation of 200.

After the first three issues, Ed abandoned the rubber-stamp-ink-pad process in favor of his father's portable typewriter and carbon copy reproduction. But his hunt-and-peck typing didn't do much to speed the output. Four issues later his parents presented him with a hectograph.

Solicits Ads

Still using this device, he is able to get as many as 250 "pretty good copies" from the gelatin slab to which he carefully transfers the impression of his typewritten carbon copy.

Beginning with the recent September issue, Ed abandoned his policy of income from limited paid circulation (20 copies at 3¢ per copy) as too unremunerative, and switched to free distribution with advertising, expanding the circulation to include many more homes on and adjacent to the reservation.

That issue of his 8½ x 11-inch, 4-page paper included a variety of newsworthy stories (See "CC Patients' Fund Enriched by NIH Children's Fair," the *NIH Record* of November 8) and a half-page ad

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British Society Invites Dr. Bunim to Deliver Its Annual Oration

Dr. Joseph J. Bunim, NIAMD's Director of Clinical Investigations, was selected by the Heberden Society to present its annual Heberden Oration on December 2 at the Wellcome Foundation, in London, England.

Dr. Bunim is one of the few Americans to be so honored since the formation of the Society in 1936. He discussed Sjorgen's Syndrome, including its relationships to rheumatoid arthritis and the other connective tissue diseases.

His paper, entitled the "Broad Spectrum of Sjogren's Syndrome and its Pathogenetic Implications," will appear shortly in the *Annals of Rheumatic Diseases*, published by the British Rheumatism Society, the English counterpart of the American Rheumatism Association.

Prior to the Heberden Oration, Dr. Bunim presented lectures on arthritis at the Universities of London and Manchester in England, at the University of Edinburgh in Scotland, and at the University of Leiden in The Netherlands.

The Heberden Society was founded in honor of an 18th Century English physician, Dr. William Heberden, Sr., who first associated osteoarthritis and rheumatoid arthritis with the enlargements and formations around the joints now known as "Heberden's nodes."

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.

NIH Studies Show Reserpine Triggers Stress Responses

Reserpine, a drug in wide clinical use as a hypotensive and tranquilizing agent, has been found to trigger certain body responses usually associated with stress: hypersecretion of ACTH, increased serum levels of glucocorticoids from the adrenal cortex, and excessive mobilization of free fatty acids from adipose tissue.

The paradox implicit in these actions of reserpine is heightened by experimental evidence that these "stress responses" 1) are produced only by doses of reserpine sufficiently large to produce overt sedation, and 2) are the indirect result of the same action of the drug believed responsible for its tranquilizing effects—depletion of brain serotonin stores.

Studies Presented

These findings were made by Drs. Bernard B. Brodie, Erik O. Westermann, and Roger P. Maickel, of the National Heart Institute's Laboratory of Chemical Pharmacology, as part of a series of animal studies on the role of the hypothalamo-pituitary-adrenocortical system in biochemical adaptation. They were presented by Dr. Brodie at the Fourth International Neurochemical Symposium, held at Varenna, Italy.

The scientists found that doses of reserpine which depleted brain stores of norepinephrine and serotonin, producing marked sedation, also provoked a sustained activation of the pituitary-adrenal system. This activation was manifested in rats by: 1) a fall in adrenal ascorbic acid, accompanied by a rise in plasma corticosterone; 2) increased activity of tryptophan peroxidase (TPO), a liver enzyme whose activity is an indicator of pituitary-adrenal stimulation; and 3) increased mobilization of free fatty acids from adipose tissue.

Similar to Stress of Cold

These responses are similar to those produced by the stress of prolonged exposure to cold, and were not produced by reserpine or cold in animals whose pituitaries or adrenals had been removed. This provided further evidence that these responses to reserpine result from pituitary-adrenal activation and are mediated by ACTH hypersecretion.

Hypersecretion of ACTH does not result from the action of reserpine *per se*, but is related to its depletion of brain serotonin stores. Doses of reserpine that deplete brain serotonin by less than 50% do not elicit noticeable sedation nor hypersecretion of ACTH; slightly larger doses elicit both responses, which become more marked with increasing doses until a maximum is reached with the complete depletion of brain serotonin stores.

That ACTH hypersecretion is related specifically to serotonin depletion has been shown by experiments using alpha-methyl-m-tyrosine. Doses of this amino acid that depleted brain norepinephrine stores with very little effect on brain serotonin, elicited neither sedation nor ACTH hypersecretion.

Responses Persist

This indirect action of reserpine also explains why the "stress" responses, like the drug's sedative effects, persist long after the administered reserpine has disappeared. Apparently, reserpine is a

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Investigator in NINDB Describes Synthesis of Long Chain Fatty Acids

The detailed sequence of biochemical reactions for the formation of long chain fatty acids in the cells of living animals has been described for the first time by a National Institute of Neurological Diseases and Blindness investigator. Fatty acids combine with glycerine to form fats, and are essential components of myelin, the fatty nerve sheath which degenerates in such disorders as multiple sclerosis.

Convert to Long Chain

In studies with purified enzyme systems from liver and brain, Dr. Roscoe Brady, Laboratory of Neurochemistry, NINDB, has shown how acetic acid, a two-carbon unit, is converted to a 16-carbon chain fatty acid known as palmitic acid.

Early studies conducted by Dr. Brady and other scientists established that the presence of carbon dioxide was essential for fatty acid synthesis. Subsequent work by Dr. Brady indicated that the key intermediate in the biosynthesis is a derivative of malonic acid, known as malonyl coenzyme A.

(See FATTY ACIDS, Page 4)

In an attempt to further identify the role of fluorides in preventing dental decay, Dr. I. Zipkin of NIDR's Laboratory of Biochemistry is studying the metabolic changes that occur in calcified tissues of the body. Experiments have shown, for example, that the normal citrate content of bone decreases markedly with an increase in fluoride. This finding suggests that fluoride competes with citrate for positions in the molecular sructure of hard tissue.

Infant Epileptics May Be Mentally Affected By Frequent Seizures

Comprehensive studies by a National Institute of Neurological Diseases and Blindness scientist of infants suffering from frequent daily epileptic seizures have led to the hypothesis that the attacks themselves may cause retardation of development in a certain category of infants.

These babies are usually under one year of age; their attacks are brief but very numerous, amounting to 30-100 or more a day; and clinical and laboratory examinations fail to reveal evidence of organic brain lesions. The last condition excludes children with brain damage in whom both epileptic attacks and retardation are caused by a *common denominator*—that is, some sort of cerebral damage.

Study Reported

Results of the preliminary study were reported by Dr. Anatole Dekaban, Section on Developmental Neurology, Surgical Neurology Branch, NINDB, in the *AMA Journal of Diseases of Children.*

All of the six infants studied had developed normally until the onset of the frequent, but usually minor, epileptic attacks, which had begun before six months of age. Extensive examinations failed to show any physical or biochemical basis for the seizures, but brain wave recordings showed abnormal electrical activity in all. These and other findings suggested that idiopathic epilepsy may occur in early infancy.

Development Slowed

A few weeks after the onset of seizures, these children displayed gradual slowing of motor and mental development, which usually was more pronounced when the attacks were most frequent.

When the seizures were controlled, however, a striking but gradual improvement in development followed. The degree of improvement seemed to be related to the age of the patient, i. e., the younger the infant when seizures were stopped or diminished, the better was the prospect for his normal development.

Dr. Dekaban speculates that seizures may slow the development of initially-normal infants by hampering alertness and natural ability to respond to and learn from environment. Lost learning opportunities at certain critical ages may never be fully regained. A need for a study of greater scope in this field is stressed.

Simple Test Found Aid In Tick Fever Diagnosis

Diagnosis of Colorado tick fever by complement fixation can be accomplished routinely in most diagnostic laboratories, according to data presented by Drs. Leo A. Thomas and Carl M. Eklund of the National Institute of Allergy and Infectious Diseases, Rocky Mountain Laboratory, Hamilton, Montana. This test, which is much simpler than any of those previously used, is described in the *Journal of Infectious Diseases.*

Virus Can Be Isolated

Previous studies from the Rocky Mountain Laboratory have shown that Colorado tick fever virus can be isolated readily from blood obtained from patients during the febrile period of their diseases, either by inoculation of suckling mice or of KB tissue culture cells, and that isolation and identification of virus is the most rapid method of laboratory diagnosis. These and other research procedures, however, are not suitable for the average diagnostic laboratory.

Drs. Thomas and Eklund, using a complement-fixing antigen prepared by Casal's technique from suckling mouse brains infected with Colorado tick fever virus, found the CF test satisfactory in detecting antibodies in serums from patients convalescent from Colorado tick fever. Complement-fixing antibodies first appeared 20 days after onset of illness, one week later than neutralizing antibodies, and were present in one patient for as long as 260 days.

Serums Available

Acute and convalescent serums were available from more than 50 patients on whom a clinical diagnosis of Colorado tick fever had been made, substantiated by isolation of virus from blood taken during the acute phase of illness and demonstration of neutralizing antibodies in blood taken during convalescence. Approximately 80 percent of those collected after the fourth week of illness contained demonstrable CF antibodies.

The authors conclude that the complement fixation test can be used successfully to detect antibodies following infection with Colorado tick fever virus. They emphasize that serums for the test should be collected four weeks or longer following onset of illness. The test should prove of value, they believe, in general diagnostic laboratories as confirmation of the clinical diagnosis of the disease.

Fluorescent-antibody stained Rickettsii in a tissue fragment of intestinal diverticulum of infected tick.

Suckling mouse brain infected with Colorado tick fever virus shows the reaction between antigenic material and labeled antibody globulin in cytoplasms of Purkinje cells.

Atabrine Found Useful In Tapeworm Therapy

A more effective treatment for beef tapeworm infestation may result from the use of atabrine administered through a duodenal tube according to Drs. Donald E. Kayhoe and Henry K. Beye of the Laboratory of Clinical Investigations, National Institute of Allergy and Infectious Diseases.

The study group consisted of 23 patients including 15 who had been unsuccessfully treated by conventional methods. A concentrated solution of atabrine was administered directly into each patient's duodenum with a Rheyfus tube.

Thirty minutes later the patients were purged with sodium sulfate solution via the tube and stools were examined for the parasite. Those who did not pass the entire parasite at this time were observed for at least one year and if stools remained negative, they were presumed cured. The regimen was successful in 20 of 23 patients studied.

Atabrine is generally well tolerated when given in this manner. No special preparation is required other than an overnight fast and in most cases the parasites are passed intact a short time after purging.

The study was reported at the meeting of the American Society of Tropical Medicine and Hygiene.

COOPERATIVE STUDY ADVANCES ACUTE LEUKEMIA KNOWLEDGE

The importance of scientifically designed studies in chemotherapy was highlighted by a collaborative study reported by National Cancer Institute investigators and their colleagues of the Acute Leukemia Cooperative Group B, sponsored by the Cancer Chemotherapy National Service Center.

During a previous study of the toxicity of a new anticancer drug, 6-azauracil, NCI scientists observed objective hematologic improvement in five leukemia patients whose disease no longer responded to conventional chemotherapy (e. g., folic acid antagonists, adrenocortical steroids, or purine analogs). A comparative study was therefore designed to evaluate the therapeutic efficacy of the drug in patients with advanced refractory acute leukemia.

Eight children and seven adults received 6-azauracil while seven children and six adults received placebo. Although partial remissions were observed for varying periods in four patients in each group, the difference between the two groups in median survival time was not significant.

Provide More Information

These findings, besides showing the importance of controlled studies in therapeutic investigations, provided an unusual opportunity to obtain information about the natural history of advanced refractory acute leukemia. A significant proportion (30 percent) of the patients showed objective hematologic improvement even in the absence of effective specific therapy. The patients had a median survival of two months from the start of the study, and children and adults showed similar survival patterns.

The toxicity of 6-azauracil limited the clinical dose to less than 10 percent of that (on a weight basis) producing antitumor effects but not toxicity in animals. These findings provide a rationale for further studies of a derivative of 6-azauracil, azauridine, which preliminary clinical studies show is better tolerated than the parent compound.

Previous Work Done

The compound, 6-azauracil, an antimetabolite, was supplied by E. R. Squibb and Sons, New Brunswick, N. J. It was synthesized in 1955 and shown to have antitumor activity in animals by Dr. Arnold D. Welch and his associates of the Yale University School of Medicine. Preliminary clinical studies reported in 1957 by scientists of the NCI and the District of Columbia General Hospital suggested that the compound had some therapeutic activity in acute leukemia.

The results of the comparative study are reported in a recent issue of *Blood* by Drs. Emil J. Freireich and Emil Frei, III, NCI's General Medicine Branch; Robert Taylor, now of the Department of Statistics, Virginia Polytechnic Institute; Edmund A. Gehan, CCNSC; James F. Holland, Donald Pinkel, and Oleg Selawry, Roswell Park Memorial Institute, Buffalo; Harvey Rothberg, Walter Reed Army Hospital, Washington, D. C.; and Farid Haurani, Jefferson Medical College, Philadelphia.

FATTY ACIDS

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As a result, Dr. Brady was able to synthesize malonyl coenzyme A by adding carbon dioxide to acetyl coenzyme A, a derivative of acetic acid. By labeling these compounds, he discovered that one molecule of acetyl coenzyme A and seven molecules of malonyl coenzyme A, combined with 14 atoms of hydrogen, are required to build a molecule of palmitic acid.

Synthesis Described

The steps in the synthesis are as follows: When acetyl coenzyme A combines (condenses), the newly added carbon dioxide is displaced. When two atoms of hydrogen are added, the resulting compound can condense with another molecule of malonyl coenzyme A. This process is repeated until the appropriate chain length is reached.

To identify the intermediates which participate in these reactions, the required enzyme systems were isolated and purified. Each step in the sequence of reactions leading to fatty acid synthesis was defined by radioactive labeling of synthetic intermediary compounds.

This basic finding, which has been presented, will be reported in the *Journal of Biological Chemistry,* and may aid in the understanding of metabolic defects associated with diabetes and degenerative disorders of the nervous system. The study will also be described to the International Biochemical Congress (Symposium on Lipid Synthesis) in Moscow, U. S. S. R., in August 1961.

"Eating a wild mushroom is as risky as Russian roulette. There's about one chance in 10 that it will cause serious poisoning," says Dr. Alexander H. Smith, a botanist at the University of Michigan.

Sensitive New System Detects Deterioration In Stockpiled Albumin

The problem of stability of normal human serum albumin during storage is of considerable practical as well as theoretical interest. For example, albumin when held in a stockpile must be able to withstand storage and shipment under various temperatures without significant change.

A long-term project has been undertaken in Division of Biologics Standards laboratories to determine what changes occur in stored albumin, the conditions affecting these changes, and the most suitable methods for detecting protein alteration. One phase of this study has been reported by Dr. J. S. Finlayson, Dr. Richard T. Suchinsky and Ann L. Dayton of the Laboratory of Blood and Blood Products.

The study was carried out on commercial human albumin preparations that had been stored for at least 5 years under various conditions. Indications were that the extent of changes occurring in albumin during storage are dependent on both the nature of the material used for preparation and the conditions of storage.

Differences Found

There was minimal difference between the chromatographic behavior of the albumin samples prepared from citrated whole plasma and stored for 5 years at 5° C and the chromatographic behavior of fresh albumin samples either prepared commercially or in DBS laboratories. However, albumin stored for ten years at 5° C or for five years at 32° C (with or without prior storage) demonstrated marked differences in chromatographic properties, as did albumin prepared from ultraviolet-irradiated dried plasma.

Fractions of albumin separated by chromatography were subjected to ultracentrifugation. The concomitant use of both techniques permitted measurement of protein components not readily observed by using either technique alone.

The clinical significance of any of the differences noted is not presently known; however, the alterations in physical-chemical character of albumin under certain conditions obviously warrant further investigation of the problem.

Studies initiated by Dr. J. T. Tripp, Chief of the Laboratory of Blood and Blood Products, using other techniques such as electrophoresis and viscosity are being continued. The work of Dr. Finlayson and co-workers indicates, however, that the chromatography-ultracentrifugation technique offers a sensitive method for the detection of protein changes in stored serum albumin.

Rapid Screening of Malaria Suspects Possible With New Fluorescent Test

A diagnostic test which may make it possible for a single laboratory worker to screen many more suspects for malaria in a given day was described at the Ninth Annual Meeting of the American Society of Tropical Medicine and Hygiene by Drs. John E. Tobie of the National Institute of Allergy and Infectious Diseases' Laboratory of Immunology and G. Robert Coatney of the Laboratory of Parasite Chemotherapy.

The new test, based on the fluorescent antibody technique, represents the first recorded instance in which a human malaria parasite (*Plasmodium vivax*) has been viewed by this method.

Fluorescent Dye Used

As in other tests of this nature, antibodies—in this instance from a serum fraction of a patient harboring the vivax type of malaria—are labeled with a special fluorescent dye (fluorescein isothiocyanate) and the fluorescent antibodies applied to a blood smear containing the malaria parasites.

The fluorescent antibody reacts with the parasite, which serves as antigen, so that when the parasites are stimulated with ultraviolet light, they glow. Prior removal of hemoglobin from the blood smear provides a slide in which the red blood cells are not visible—essentially just the glowing malaria parasites.

To evaluate the new procedure, the scientists tested blood smears from seven inmate volunteers known to harbor the vivax type of malaria parasite. Under the fluorescence microscope, each specimen of the prepared parasite—glowing a bright yellow color—stood out clearly from the rest of the field.

Other Parasite Visualized

Using the same procedure, the investigators were able to visualize the parasite of monkey malaria (*Plasmodium cynomolgi bastianellii*) with the same clarity of detail.

Serological tests, such as complement fixation, precipitin or agglutination tests for the diagnosis of malaria, essentially have been of no practical value. For such diagnosis, it has been necessary that well-trained technicians spend many hours in the examination of conventionally stained blood smears.

With the new procedure, a far more rapid method of screening is within the realm of possibility. The picture presented under the fluorescence microscope is such that it may be possible for a photo-electric cell to detect the glowing parasites. For this reason, the scientists are currently exploring the possibility of feeding slides of individual test specimens serially through an electronically controlled automatic scanning microscope for the detection of parasites in large-scale surveys.

Studies Are Preliminary

The scientists emphasized that their studies were strictly of a preliminary nature and that many technical difficulties must be solved before their goals may be achieved.

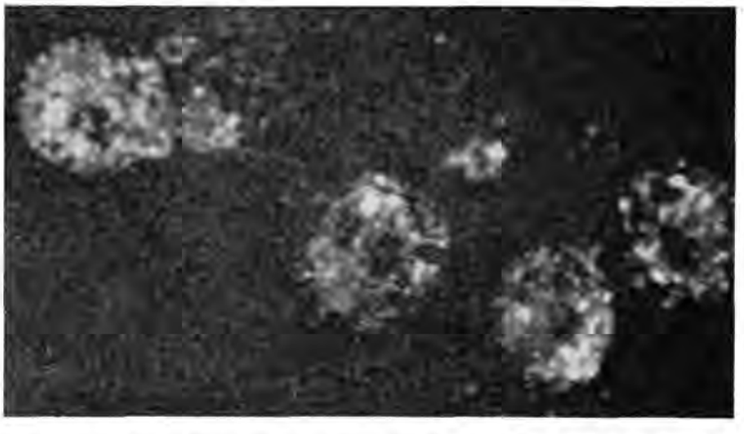
As a part of their study, the investigators observed the serological relationships between a human malaria parasite, *P. vivax*, and a rodent malaria parasite, *P. berghei*. When viewed under the fluorescence microscope, the former glowed approximately three times as bright as the latter, suggesting a distinct difference between the two species.

However, when the human type (*P. vivax*) was compared with the parasite of monkey malaria (*P. cynomolgi bastianellii*), both species glowed at essentially the same intensity indicating that they may be closely related malaria parasites.

Despite the relative success of the World Health Organization program to eradicate malaria, nearly half of the world's population continues to live in areas of exposure.

Coming at the present time, the new procedure assumes an added significance in view of the further diagnostic difficulties now being imposed on the already overburdened technician with the recent discovery that monkey malaria may provide a permanent reservoir for the disease.

Photomicrograph of Plasmodium vivax under ultraviolet light.



Photomicrograph of Plasmodium synomogli bastianellii under ultraviolet light.

RESERPINE

(Continued from Page 3)

"hit-and-run" drug which depletes the brain of its amines by inactivating or destroying their storage sites. The brain amines remain depleted until the storage sites recover, when brain amines slowly return to normal. The "stress" responses will persist until brain serotonin again reaches 50% of normal.

These studies point out the potential value of pharmacological tools in clarifying how the brain directs biochemical mechanisms, and that the interaction of drugs with these mechanisms may be an important aspect of drug action.

NIAID Scientists Report Findings On Amebiasis

Results of a survey of State Department employees reveal a surprising lack of correlation between infection with *Entameba histolytica* and job absenteeism, weight loss or excessive reports of diarrhea and abdominal pains.

The survey was carried out jointly by Drs. Donald E. Kayhoe, Henry K. Beye, and Elizabeth Guinn of the National Institute of Allergy and Infectious Diseases' Laboratory of Clinical Investigation; and Dr. George P. George of the State Department. It involved nearly 6,000 of the more than 35,000 employees and dependents stationed outside the United States.

Local Facilities Used

Most of these individuals relied on local facilities for food, water, sanitation, and medical care. Frequently their meals were prepared according to the prevailing culinary and sanitary customs. Sixteen percent reported no running drinking water in their place of residence and almost all employed local household servants.

Each participant submitted a stool specimen which was forwarded to the National Institutes of Health for study. Those requiring treatment were handled either at Bethesda or the Department of State facilities. Laboratory findings were correlated with replies to questionnaires to provide a rough measurement of the effects of intestinal parasitism on the health of these individuals during their assignment overseas.

Answers to one of the questionnaires on health status were compared against individuals free of parasites, and those harboring *E. histolytica* or *Giardia lamblia*. While more of those with *E. histolytica* believed their health was poorer than usual, little difference was found between the three groups in respect to time lost from work. Diarrhea was commonplace, yet, surprisingly, the sufferers included almost as many harboring the ameba as without.

Questions Raised

The authors of the report, which was presented to the American Society of Tropical Medicine and Hygiene, emphasize that their results do not in any way minimize the importance of amebiasis as a disease. More questions have been raised than have been answered and further investigations must be undertaken to gain an adequate understanding of its pathogenesis.

At one time, the presence of the parasite was always assumed to be synonymous with overt symptoms of disease. This is now known to be false. Other recent investigations have implicated climatic or dietary factors—or bacteria living in the gastrointestinal tract—as possible trigger mechanisms for converting the benign parasite into a virulent one.

Whatever the truth, the present study is expected to make a significant contribution to the rapidly changing picture of this disease—about which only two broad facts appear to be beyond challenge at the present time: its distribution is world-wide and its clinical manifestations, very broad.

Plasma Antagonist to Insulin Found in Untreated Diabetes

The presence of substances antagonistic to insulin in the plasma of patients with diabetes mellitus who have never received insulin therapy has been shown in recent studies by Dr. James B. Field, Clinical Endocrinology Branch, National Institute of Arthritis and Metabolic Diseases.

These studies shed provocative light on an important possible cause of diabetes other than pancreatic inability to produce insulin.

The likelihood that many cases of diabetes are due to substances in the patient's body which interfere with provision of an effective insulin concentration to peripheral tissues has been considered by endocrinologists for many years.

A cause of diabetes of this sort is under investigation because numerous diabetic patients require more than forty units of insulin a day, the level needed by a patient whose pancreas has been removed in the treatment of some other disease and whose diabetes is thus due to his inability to produce his own insulin.

Inhibitors Found

Inhibitors or antagonists to the action of insulin having the properties of antibodies have previously been found by Dr. Field and by other investigators in the plasma of patients with chronic insulin resistance requiring amounts of insulin in excess of two hundred units per day.

Temporary insulin resistance, accompanied by the presence of increased amounts of inhibitors, has also been found in diabetic acidosis or coma, and during infection. In general there has been no good correlation between the titer of insulin antibody and a patient's daily insulin dosage.

The recent NIAMD studies of Dr. Field differ from previous observations in that insulin antagonist was detected in the plasma of two of four new diabetic patients prior to insulin therapy, indicating the presence of a substance interfering with the action of insulin which is not an antibody elaborated in response to administered insulin.

Clinically, there were no distinguishing features between the two cases with antagonist and those without. They all had high blood sugars, large amounts of sugar and ketone bodies in the urine without severe acidosis and required insulin for control of their diabetes in approximately equal amounts. Inhibitor could no longer be detected once the diabetes was controlled.

Detection of this apparently new type of insulin antagonist in the NIAMD studies provides a lead for further investigation of a variety of factors affecting insulin production, binding, transport and action at the peripheral tissue level.

The possibility exists that the antagonist is a hormone of pituitary origin, perhaps related to growth hormone. The studies, and a review of factors affecting insulin reaction, were reported by Dr. Field in *The Journal of the American Diabetes Association*.

This is Volume 1, Number 1 of a new journal to be published bimonthly for the Biophysical Society. Easily identified by its modern gray and red cover, the journal is published by the Rockefeller Institute Press, N. Y. The publishers expect the new journal to be of interest to scientists in the fields of biology and physics. Among the authors and titles appearing in the first (September) issue are: Kenneth S. Cole and John W. Moore, "Potassium Ion Current in the Squid Giant Axon: Dynamic Characteristic;" George L. Gerstein and Nelson Y-S Kiang, "An Approach to the Quantitative Analysis of Electrophysiological Data from Single Neurons." Dr. Cole is Chief and Dr. Moore is Assistant Chief of the Laboratory of Biophysics, NINDB.

NCI Reports Results On Leukemia Study

National Cancer Institute scientists have reported the results of a comprehensive study of meningeal leukemia, which was observed in 25 of 150 acute leukemia patients admitted consecutively to the Clinical Center during a five-year period ending April 1, 1958.

Findings reported previously by the same investigators showed that meningeal leukemia develops as a result of infiltration of the arachnoid by leukemic cells. The infiltration apparently interferes with the flow of cerebrospinal fluid, resulting in increased fluid pressure and hydrocephalus.

Meningeal involvement is primarily a complication of acute lymphocytic leukemia in children. The syndrome may occur at any stage of the disease: as an initial manifestation, during hematologic remission, or during an active leukemic phase.

A diagnosis of meningeal leukemia is confirmed by examination of the cerebrospinal fluid showing increased pressure, presence of leukemic cells, and absence of infection. The characteristic radiologic finding is spreading of the cranial sutures in children.

A literature review included in the present report shows that meningeal luekemia has become more common since the advent of chemotherapy. Only 31 patients were reported between 1878 and 1948, in contrast to 69 between 1949 and 1959.

Antimetabolites Have Role

The increase is partly related to the ability of antimetabolites to prolong the lives of acute leukemia patients, particularly children. Of 21 children in the Clinical Center group, 13 developed the meningeal syndrome more than four months after onset of leukemia. It appears that the failure of antimetabolites to cross the "blood-brain barrier" may play a role in the development of the meningeal syndrome.

The investigators recommend treating meningeal leukemia first with adrenal steroids administered systemically; then, if additional therapy is indicated, with whole brain irradiation, or methotrexate injected into the spinal fluid.

The findings are reported in a recent issue of *Neurology* by Dr. Richard K. Shaw, now of the University of Washington Medical School, Seattle; Dr. Edward W. Moore, now of Boston City Hospital; Dr. Emil J. Freireich, NCI's General Medicine Branch; and Dr. Louis B. Thomas, NCI's Department of Pathologic Anatomy.

EDITOR ED

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that cost a Bethesda toy shop 65 cents.

With the other half of that page unsold, Ed devoted it to self-advertising: "STATION TRIBUNE now reaching 200 homes. Your ADS get BETTER Results FASTER."

In fact, Editor Ed progresses so fast it's hard to keep track of him. Only last week he walked into the *Record* office with a copy of his latest issue, revealing a "tabloid" format.

He has reduced his page size to one-half and doubled the number of pages to eight. At the same time he more than doubled his advertising rates: 70¢ for the new size half-page, 40¢ per quarter-page, etc.

Business Is Good

In spite of this the latest issue has a full page of ads—the same toy shop (½ page), a Bethesda barber shop (¼ page), and two "For Sale" items (⅛ page each). The next issue, Ed says, will also carry classified ads at 5¢ per column line.

Ed attributes much of this mounting commercial success to his recently acquired advertising manager, Rod Shane, 13, of Bethesda, whose father heads a Washington advertising agency.

His present staff also includes his younger brother, Dick, 11, who collects news items and helps deliver the paper.

Ed also has a sister, Marilyn, 11 (Dick's twin), and another brother, Stanley, 6. It is just possible that some day they might fit into the expanding scheme of things, provided they have what it takes.

Ed himself is now the Managing Editor, and like many another newspaperman he likes to look back occasionally and reminisce a bit.

Scores a 'Beat'

He gleefully recalls, for instance, the time last year when he scored a "beat" not only on the *Record* and the county weeklies but the Washington dailies as well.

Dr. Arthur Kornberg, Chairman of the Department of Biochemistry, Stanford University, and former Chief of the Enzyme and Metabolism Section of NIAMD, had been selected to deliver the Ninth NIH Lecture on October 13 and was the house guest of his friends and former colleagues, Ed's parents.

Following Dr. Kornberg's departure on October 14, Ed overheard his parents discussing the possibility that Dr. Kornberg might well be a candidate for one of the international Nobel Awards, to be announced the following day.

With suitable space reserved in the *Station Tribune* of October 15, Ed on that day stayed glued to the radio newscasts.

Sure enough, the 12 o'clock noontime news carried the announcement that Dr. Kornberg had been named with Dr. Severo Ochoa of the New York University College of Medicine as co-winner of the 1959 Nobel prize in medicine.

Ed promptly hammered out his big lead story, hectographed it into the allotted space, and had the *Station Tribune* "off the press and on the street" by 1:15 p.m.

And he didn't even call it an Extra Edition.

35 Challenge Chess Expert; 2 Win, Boy Displays Ability

In a simultaneous chess exhibition here last week, Dr. Eliot Hearst, NIMH research psychologist and member of the U. S. chess team that won the World's Student Team Championship last summer, took on 35 challengers and defeated 31 of them.

Two of the challengers won their games against the young Chess Master and two contests were declared draws.

The winning challengers were Dr. Milton Wittman of the NIMH Training Branch and Jurgis Blekaitis of the Voice of America. Mr. Blekaitis was one of nine guest competitors. Three others were Clinical Center patients, and the remaining 23 were NIH personnel.

Boy, 12, Plays Well

One of the challengers whose play won praise from Dr. Hearst was a 12-year-old boy, Peter Graves, son of Corinne Graves, DGMS information specialist and a staff correspondent of the *Record*.

At the conclusion of the exhibition, Dr. Hearst told Peter that his first 25 moves were "perfectly played." Mrs. Graves said Dr. Hearst later told her by telephone that her son had displayed unusual ability and that with proper coaching he "could look to a future in chess."

Mrs. Graves later told the *Record* that although Peter was greatly pleased he was "taking it all in stride," and for the present planned to continue chess only as a hobby.

Peter is a student at the Landon School for Boys in Bethesda and is primarily interested in science, especially astronomy. He has been playing chess with his father for three years, Mrs. Graves said.

Dr. Hearst was the subject of an NIH Spotlight feature in the *Record* (Aug. 30), following his return last summer from Leningrad, where the seven-man U. S. team walked off with the international student team championship, defeating the second-place Russian team by 1½ points for the first loss of a world match by the Russians in 25 years.

Qualifies for Team

Dr. Hearst is a staff member of the Clinical Neuropharmacology Research Center at St. Elizabeths Hospital. He was young enough—by six days—to meet the 28-year maximum age limitation last July 1 for qualification as a member of the U. S. student team.

The NIH chess exhibition, held Monday evening, November 28, in the Building 1 cafeteria, was conducted by the R&W-sponsored NIH Chess Club, which meets there each Monday evening at 7:30.

The club president, Dr. Roy Repaske, staff member of the NIAID Laboratory of Infectious Diseases, says that players of all levels of proficiency are welcome and instruction is offered to beginners. For additional information, call Dr. Harold Baer, secretary-treasurer, Ext. 3045.

The young Chess Master, Dr. Eliot Hearst of NIMH (left), makes a move in his game with Dr. Howard Schwartz of NCI, one of 35 challengers he engaged in a simultaneous chess exhibition here last week. The youngest challenger, 12-year-old Peter Graves (right), ponders strategy between moves.—Photos by Jerry Hecht.

Dr. Soper Named Head Of Pakistan-SEATO Cholera Research Lab

Dr. Fred Lowe Soper, an NHI Visiting Scientist, has been named Director of the Pakistan-SEATO Cholera Research Laboratory at Dacca, East Pakistan. His appointment was announced on December 5 by Pote Sarasin, Secretary-General of the South East Asia Treaty Organization.

Dr. Soper

Dr. Soper retired recently as Director of the Pan American Sanitary Bureau and Regional Director of the World Health Organization. He is internationally known for his work on control of malaria, yellow fever, and typhus fever, having served previously with the International Cooperation Administration and the Rockefeller Foundation in these fields.

The appointment of two senior members to Dr. Soper's staff at the Laboratory in Dacca was also announced.

Dr. Joe L. Stockard, a PHS Commissioned Officer, will head the Epidemiology Laboratory and serve as Deputy Director, and Dr. Kazi Abul Monsur, of the Government of East Pakistan, will head the laboratory's Bacteriology Section.

The Cholera Research Laboratory, dedicated on December 5, occupies space made available by the Government of Pakistan.

The services of certain technical and administrative personnel have also been provided by this Government. Special laboratory equipment has been purchased by NIH with funds allocated by the U. S. and the United Kingdom.

CHANGES

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career officer since 1943. His first PHS assignment brought him into malaria control in the War Areas Program. In 1948 he was appointed Chief of the Service's field station in Thomasville, Ga., where he remained until his transfer to DRG in 1953 as Chief of the Program Analysis Section. In 1955 he became DRG Scientific Director, and in 1957 his position was renamed Assistant Chief.

Dr. Powell has been a member of the PHS Commissioned Officers Corps since 1946. Prior to becoming Assistant Grants Branch Chief for Clinical Research, he served as Executive Secretary to the Radiation and Surgery Study Sections, and in 1956 headed the PHS Radiological Health Medical Program, Division of Special Health Services.

Dr. Silbergeld, DGMS, Appointed as Chief Of New Section

Dr. Sam Silbergeld, Program Analyst in the Research Grants Branch, DGMS, has been named Chief of the Division's recently established Clinical Research Center Section.

The new section, which is within the Research Grants Branch, headed by Dr. Carl R. Brewer, will handle applications for general clinical research centers coming under the responsibility of DGMS. It will conduct preliminary negotiations and staff visits; aid in the review of grant applications; assist the National Advisory Health Council in matters pertaining to the general Clinical Research Center program; handle professional requests for information on the program; and maintain continuing liaison with established Centers.

Dr. Silbergeld

A senior surgeon in the PHS Commissioned Corps, Dr. Silbergeld has been associated with NIH since 1956. Before transferring to DGMS last November, he was a staff assistant to Dr. Roderick Murray, Director of DBS.

Library to Step Up Translation Service

The NIH Library is taking immediate steps to reduce a mounting backlog of requests for scientific translation service. This action is in response to a recent recommendation by the Scientific Directors.

High priority requests will take precedence over all others; requisitioning procedures are undergoing revision, and other changes are being planned by John J. Clopine, NIH Librarian, and Rosemary Roberts, Translating Section Chief.

Miss Roberts urges personal discussion of each translation request to help reduce the backlog and to clarify the extent of translation necessary in the future. Her extension is 2257.

The Translating Section said it is prepared to give immediate oral service and to provide quick, rough translations of foreign language articles.

Translations can be provided from 20 languages including the Romance, Germanic, Slavic, Scandinavian, and Japanese languages.

Beginning January 1, recorded oral translations will require the approval of Laboratory or Branch Chiefs, and written translations will require the approval of Scientific Directors or Division Chiefs.

DR. DYER ATTENDS DYER LECTURE

On the occasion of the tenth in the series of annual R. E. Dyer Lectures established in his honor, Dr. Rolla E. Dyer, Director of NIH from 1942 to 1950 (left), returned here November 15 to attend the lecture presented by Dr. George Macdonald, Director of the Ross Institute of the London School of Tropical Medicine (center). With Dr. Justin M. Andrews, Director of NIAID, they met before the lecture in the office of the CC Director, Dr. Jack Masur. The R. E. Dyer Lectureship was originally suggested by Dr. Norman Topping, Associate Director of NIH during Dr. Dyer's tenure of office and now President of the University of Southern California. Dr. Topping was at NIH prior to the lecture but was unable to attend because of previous commitments.

End of UGF Campaign Finds NIH Below Quota

The UGF campaign, extended for an additional week, came to an end officially on November 28. Ninety-nine percent of NIH employees participated, contributing a total of $67,168. This figure represents 85 percent of the $79,305 goal.

According to Dr. Roderick Murray, campaign chairman, this goal is 31 percent higher than last year's figure. "Though NIH has contributed $4,500 more this year than last," Dr. Murray said, "the goal is not yet met, and the need for funds still exists."

5 Units Reach Goal

Five NIH units had reached or exceeded their goal by the last week of the campaign. DGMS was still in the lead with 135 percent, NIDR reached 104, DBS had 103, DRG had 101, and NIMH reached 100 percent.

The campaign, originally scheduled to terminate on November 21, was extended after an appeal from DHEW Secretary Flemming, who spoke to NIH keymen at a special meeting in the CC auditorium on that date.

Secretary Flemming pointed out that although almost all NIH employees had contributed to the campaign, the average gift was slightly smaller than last year. Therefore he suggested an additional gift of $5 each from those who were able to give.

"It is important to reach our goal during Thanksgiving week," said Secretary Flemming. "In the spirit of Thanksgiving we are giving people the opportunity of expressing their own thankfulness by helping their fellow human beings."

A breakdown of the final figures follows:

	Percent of Participation	Amount Contributed
OD-NIH	119	$5,601
DRS	105	6,343
DRG	103	4,113
DGMS	124	1,213
DBS	108	2,097
CC	103	8,831
NCI	82	8,990
NHI	101	5,010
NIAID	94	4,022
NIAMD	102	7,353
NINDB	82	3,292
NIMH	93	8,138
NIDR	113	2,164
Totals	99%	$67,168

Mrs. Graber Appointed To DGMS Position

Mrs. Joe E. Graber, of Bethesda, has been appointed Information Officer for the Center for Aging Research, DGMS. Her office is located in the Trunnell Bldg., Cordell Ave., Bethesda.

Mrs. Graber worked with the PHS in health education and as an administrative analyst from 1943 to 1949 in Washington, D.C., Louisiana, and Georgia. She has also worked for the Louisiana State Department of Health, the Massachusetts State Department of Health, the District of Columbia Tuberculosis Association, and Suburban Hospital in Bethesda.

A graduate of Louisiana State University, Mrs. Graber received an M.P.H. degree from Yale University School of Medicine in 1945.

Annie's Marksmanship Highlights Hamsters' Musical Next Month

"Annie Get Your Gun," the Hamsters' musical comedy production for this season, is scheduled for presentation some time in January.

Technical problems still to be solved are all that hold up announcement of the dates, according to Dr. Arnold W. Pratt, producer.

Tickets, at $1.50 each, go on sale this month through R&W representatives and at the film desk and CC post office.

The Hamsters chose "Annie" because of its gaiety, lively music, and happy theme.

Music by Berlin

With music by Irving Berlin and book by Herb and Dorothy Fields, "Annie" opened in New York in 1946 with Ethel Merman in the title role. It had a long run on Broadway and still turns up in road shows, TV, and little-theater productions.

The show has a typical boy-meets-girl, boy-loses-girl, boy-gets-girl plot.

Annie Oakley, played at NIH by Verece Silverman, joins Buffalo Bill's Wild West Show as a marksman, and finds herself competing with Frank Butler (Maryland U.'s James Kinnamon).

Budding love turns into anger, after a brilliant display of shooting by Annie, who then tours Europe with the Buffalo Bill Show while Frank joins a troupe that subsequently fails.

True Love Triumphs

Eventually the two wild-west shows and the hero and heroine merge, providing a tuneful, happy ending.

Several sub-plots and colorful characters round out the show. Charlie Davenport (Ozzie Grabiner) and Dolly Tate (Bobbie Dubois) provide subsidiary love interest, and Winnie (Betsy Slay) and Tommy (Dr. Robert Fouty) are the ingenue and her "fellow."

The wild west flavor comes in heavy doses from Sitting Bull (Billy Sadesky) and Buffalo Bill himself (Peter Lord).

And, of course, girls. Girls who sing and dance, and men who do the same.

The show's first performance will be given exclusively for CC patients, their relatives and friends.