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DR. FREUND HONORED BY ALLERGY GROUP

Dr. Jules Freund, Chief of the Laboratory of Immunology, NIAID, was awarded a special citation last month by the Allergy Foundation of America, honoring him for his outstanding contributions to medical science.

The development of an adjuvant that is a routine tool used in basic laboratory research by immunologists all over the world, was cited particularly. Freund's adjuvant is a water-in-oil emulsion that increases the protective effect in vaccines.

The main emphasis of Dr. Freund's work in preventive medicine has been in basic research. His studies of antibody formation, allergy, toxin-antitoxin reactions, and demyelination are fundamental to the work of many laboratories today.

Before joining NIH in 1957, Dr. Freund was chief of the Division of Applied Immunology, Public Health Research Institute of the City of New York.

DR. KNIGHT JOINS NIH IN ALLERGY RESEARCH

Dr. Vernon Knight has been appointed Chief of the Laboratory of Clinical Investigation, NIAID. He assumed his new post July 1. Dr. Knight was formerly director of the George Hunter Laboratory for Study of Infectious Diseases, Vanderbilt University Medical School.

Dr. Knight will also serve as the Institute's clinical director, supervising the planning and conduct of a broad program of patient-centered studies on allergic and infectious diseases.

While at Vanderbilt, Dr. Knight headed clinical and laboratory research programs, with special emphasis on antibiotic-resistant staphylococcal infections.

Dr. Knight received his M.D. degree from Harvard Medical School in 1943. From 1950 to 1954 he was director of the Laboratory of Infectious Diseases, Cornell Medical Division, Bellevue Hospital, New York.

PHS EMPLOYEES INFORMED ON NEW 'TRAINING ACT'

A six-page pamphlet of questions and answers pertaining to the "Government Employees Training Act" (Public Law 85-507) is being distributed to all PHS employees during the month of August. It provides basic information regarding training at non-Government facilities. The act authorizes Federal agencies to establish training programs for the development of Civil Service employees in order to increase economy and efficiency in Government operations.

While the law permits training of Federal employees at Government expense, it does not entitle any employee to such training. All training must be work-related and justified, and must meet PHS needs for specific skills.

The pamphlet outlines means, procedures, and prerequisites for application, and lists Federal Personnel Manual references.

At NIH, further information is available from Institute and Division administrative officers.

INSTRUMENT EXHIBIT PLANS READIED



Local representatives of manufacturers met with officials here last month to plan display space for the annual instrumentation symposium, to be held at NIH, September 28 - October 1. Left to right: Richard W. Lyons, Rockville; James B. Davis, Chief, Supply Management Branch, DBO; Louis R. Heiss, Silver Spring; Norman E. Bengston, Washington; Donald W. Metz, Falls Church.

NCI Plans Conference On Anticancer Drugs

The Cancer Chemotherapy National Service Center, NCI, is planning a two-day conference on clinical anticancer drug research to be held in Washington, at the Hotel Statler, November 11-12.

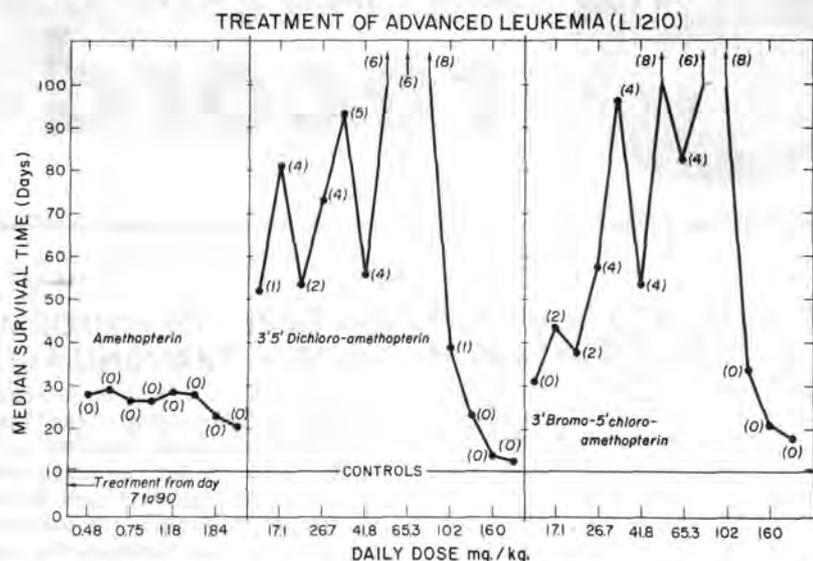
Many of the nation's leading cancer chemotherapy investigators have been invited to participate. Approximately 1,000 physicians and scientists are expected to attend.

Mr. Harlow Retires

Roy L. Harlow, Chief Finance Officer, PHS, retired last month after 30 years of Federal Service.

New Drugs Check Leukemia In Mice

No. 230 in a Series



The efficacy of amethopterin and two of its derivatives in treating mouse leukemia is shown above. The median survival time of ten mice is shown at each dosage level. Figures in parentheses are the number of 100-day survivors. Survival in excess of 100 days is shown by arrows pointing upward.

Striking increases in the survival time of mice with advanced leukemia have been effected with two new drugs derived from amethopterin (methotrexate)--a compound now in use for the treatment of acute leukemia.

Mice within a few days of death from leukemia have been presumably "cured" or their lifespans extended significantly with these derivatives, known as 3'-bromo-5'-chloroamethopterin and 3',5'-dichloroamethopterin. As a result of these promising studies, the latter compound is now undergoing preliminary clinical trial in the NCI research program and under the auspices of the Cancer Chemotherapy National Service Center.

The discovery of the effectiveness of the drugs is the result of systematic investigations of chemotherapeutic agents conducted by NCI's Laboratory of Chemical Pharmacology. An improved assay procedure was developed in which treatment of leukemia L-1210 in mice is withheld until the disease is widely disseminated and death is imminent. The effectiveness of the drugs is then evaluated by measuring the increase in survival time of the mice.

In earlier tests with a group of 38 drugs, the greatest increase in survival time was consistently produced by methotrexate. The new derivatives, however, have produced

survivals three to four times greater than did methotrexate.

Dr. Abraham Goldin and his associates became interested in these compounds when they observed that halogenated (combined with chlorine and bromine) derivatives exhibited greater antileukemic influence than methotrexate. When the derivatives were purified, their antileukemic effectiveness was increased. Halogenation also increased the amount of the drug that the animals could safely tolerate.

When the halogenated derivatives were administered to mice at optimal treatment levels, they produced median survival times of 90 days and more from the date of inoculation with leukemic cells. This is particularly noteworthy considering that the animals would have died of leukemia in two to three days if untreated. The median survival time with methotrexate was 20 to 30 days, even when treatment was started early in the course of the disease.

Some of the animals treated with the new compounds have lived as long as six months after inoculation and appear to be "cured." Whether or not they still harbor leukemic cells has not as yet been determined. When these animals were reinoculated with leukemia, however, the disease did not develop,

(See *Leukemia*, Page 3)

Publication Preview

The following manuscripts were received by the SRB Editorial Section between March 9 and March 19.

NCI

Andrews, H. L. Survival time following massive fractionated irradiation.

Blum, H. F. Quantitative aspects of cancer induction and growth: As illustrated in carcinogenesis by ultraviolet light.

Charache, S., Condit, P. T., and Humphreys, S. R. Studies on the folic acid vitamins. IV. The persistence of amethopterin in mammalian tissues.

Charache, S.; Condit, P. T.; Levy, A. H.; Humphreys, S. R.; and Goldin, A. Studies on the folic acid vitamins. V. The effect of folic acid on the citrovorum factor activity of mouse liver.

Condit, P. T. Studies on the folic acid vitamins. II. The acute toxicity of amethopterin in man.

Condit, P. T. Studies on the folic acid vitamins. III. The duration of the effects of the folic acid antagonists in man.

Hueper, W. C., and Payne, W. W. Experimental cancers in rats produced by chromium compounds and their significance to industry and public health.

Ketchum, A. S. The use of a hypochlorous acid derivative in the control of cancer: An animal investigation of seeded wounds.

Langan, T. A.; Kaplan, N. O.; and Shuster, L. Formation of the nicotinic acid analogue of diphosphopyridine nucleotide following nicotinamide administration.

NHI

Long, R. T. L.; Waldhausen, J. A.; Cornell, W. P.; and Sanders, R. J. The detection of right-to-left circulatory shunts: A new method utilizing injections of a radioactive gas, Kr⁸⁵.

Ross, J.; Braunwald, E.; and Morrow, A. G. Transeptal left atrial puncture: A new method for the measurement of left atrial pressure in man.

NIAMD

Eyles, D. E.; Gibson, C. L.; Coleman, N.; Smith, C. S.; Jumper, J. R.; and Jones, F. E. The prevalence of toxoplasmosis in wild and domesticated animals of the Memphis region.

Habel, K. The nature of viruses and viral diseases.

Kilham, L., and Olivier, L. J. A latent virus of rats isolated in tissue cultures.

Munoz, J.; Ribí, E.; and Larson, C. L. Antigens of *Bordetella pertussis*. I. Activities of cell walls and protoplasm.

Utz, J. P., and Bell, N. H. Proceedings of combined Clinical staff meeting. Sarcoidosis.

Vargosko, A. J.; Chanock, R. M.; Huebner, R. J.; Luckey, A. H.; Kim, H. W.; Cumming, C.; and Parrott, R. H. Association of type 2 hemadsorption (parainfluenza 1) virus and Asian influenza A virus with infectious croup.

von Brand, T. Influence of oxygen on life processes.

NIAMD

Allison, A. C., and Blumberg, B. S. Ability to taste phenylthiocarbamide among Alaskan Eskimos and other populations.

Altland, P. D.; Highman, B.; and Roshe, J. Effects of altitude on dogs with valvular heart disease. Tolerance and pathologic effects of acute and chronic exposures.

Edelhoc, H. The denaturation of pepsin. IV. The effects of temperature.

Field, J. B. On the nature of the metabolic defect(s) in diabetes.

Labaw, L. W. An electron microscopic determination of the Rothamsted tobacco necrosis protein crystal structure.

Robbins, J., and Rall, J. E. Distribution and metabolism of thyroid hormone.

Stohlman, F., Jr., and Brecher, G. Effect of bone marrow activity on erythropoietin utilization.

NIDR

Arnold, F. A., Jr. The National Institutes of Health Graduate Training and Fellowship Programs.

Lyman, F. E. Research developments.

McCann, H. G. Determination of microgram quantities of magnesium in mineralized tissues.

NIMH

Bradey, W. M. Narcissistic relationship - a paradox.

Bowen, M. Family psychotherapy.

Dysinger, R. H. Study and treatment of the family unit; a family perspective on the diagnosis of individual members.

Fisher, S. Child research in psychopharmacology.

Fleming, T. C., and Evarts, E. V. Multiple response to photic stimulation in cats.

Knee, R. I. Recent advances in the treatment of the mentally ill.

Mirsky, A. F., and Rosvold, H. E. The use of psychoactive drugs as a neuropsychological tool in studies of attention in man.

Mishkin, M. Effects of cortical lesions in monkeys on critical flicker frequency.

Hewitt, R. T. Current trends in the care of the mentally ill.

Jacobson, S. "Ideal" school conditions--their meaning for educational process.

NINDB

Agranoff, B. W.; Eggerer, H.; Henning, U.; and Lynen, F. Isopentenyl pyrophosphate isomerase.

Bailey, C. J., and Guth, L. Role of the sympathetic nervous system in the pupillary response to darkness.

Cammermeyer, J., and Swank, R. L. Acute cerebral changes in experimental canine fat embolism.

Fuortes, M. G. F. Discontinuous potentials evoked by sustained illumination in the eye of *Limulus*.

Miquel, J. A simple and rapid stain for biopsy of brain tumors.

Moore, J. W., and del Castillo, J. An electronic electrode.

Peters, E. L.; and Tower, D. B. Glutamic acid and glutamine metabolism in cerebral cortex after seizures induced by methionine sulfoximine.

Resnik, R. A.; Wanko, T.; Gavin, M. A.; and Kenton, E. Small cytoplasmic elements in lens fibers. Integrated biochemical and electron microscopic observations.

Rice, E. C., and Dekaban, A. S. Congenital hemiplegia resulting from cerebral malformation. Terminal complication of myeloid leukemia.

Tasaki, I. Demonstration of two stable states of the nerve membrane in potassium-rich media.

Tower, D. B. Neurochemistry of epilepsy. Seizure mechanisms and their management.

Windle, W. F. Atlas of the dog brain.

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NIH Spotlight



Dr. Joseph E. Hayes, Jr.

Dr. Joseph E. Hayes, Jr., biochemist in NHI's Laboratory of Technical Development, describes himself as a "second-generation chemist." He remembers assisting in his chemist-father's lab when he was barely big enough to reach to the table top. Today, he spends most of his time working with a special-purpose analog computer developed in conjunction with his laboratory associates, Frank W. Noble and Dr. Murray Eden.

"What this machine does for a living," Joe Hayes explains, "is to break down curves, which are sums of a known distribution function, into their components. We can take an absorption spectrum and resolve it into the individual absorption bands, or we can resolve an electro-phoretic pattern into its individual components."

Joe received his Ph.D. degree in biochemistry at Washington University, in St. Louis, and then went on to the Johnson Foundation for Medical Physics, at the University of Pennsylvania, where he did research on the kinetics of rapid enzyme reactions.

During an army tour at Walter Reed Army Medical Center, he worked on the metabolism of rickettsiae and on the mode of action of antibiotics. While there, he became interested in spelunking (exploration of caves), and made a number of expeditions to the Virginia and West Virginia mountains, where caves abound.

But Joe's present explorations take him on a more horizontal route along parts of the C&O Canal, which he considers one of the most attractive features of the Washington area.

Another of his avocations, slightly less energetic, is singing. He pres-

NEWS BRIEFS

Mark D. Hollis, Chief Engineer, Division of Sanitary Engineering Services, has been appointed to the newly created position of Associate Chief for Sanitary Engineering, Bureau of State Services, PHS.

Dr. G. Gilbert Ashwell, NIAMD, has replaced Dr. Leon Heppel as Chief of the Section on Enzymes and Cellular Biochemistry in the Institute's Laboratory of Biochemistry and Metabolism. Dr. Heppel was recently named Chief of the laboratory.

Portable dental equipment which may enable dentists to give home or bedside treatment to disabled persons is being tested by PHS. The equipment consists of two 45-pound cases of instruments that can be operated from an ordinary household outlet.

LEUKEMIA Contd.

suggesting that they may have become immune.

According to Dr. Goldin, the results of these studies provide "an experimental demonstration of the feasibility of long-term control of systemic leukemia by drugs." The experiments also show the importance of systematic studies of compounds closely related to drugs of known activity. Working with Dr. Goldin in this study were Stewart R. Humphreys and John M. Venditti, Laboratory of Chemical Pharmacology, and Nathan Mantel, Biometry Branch.

ently serves as chairman of the NIH Chorus, and is also a member of the Walter Reed Chapel Choir.

Almost sedentary, by comparison, is the clock and organ repairing and restoring that Joe undertakes for fun. What he describes as a long-standing love for gadgets led him to restore an old reed organ and two Seth Thomas clocks. All three are now functioning in his home, good as new. And he is hoping to find a small pipe organ in restorable condition for further tinkering.

The future? "I'm doing work that's very interesting--to me, at least--and which I think is important. When we get some current computer problems squared away, there are a number of things I'd like to look into that are closer to work I have done in the past..."

NEW GRAY LADY CHIEF



Mrs. Anna Headley

Mrs. Anna Headley, of Rockville, Md., has been appointed Chairman of the NIH Gray Ladies. She succeeds Mrs. Kaye Eschmeyer, who had served since July 1958.

Mrs. Headley has been active in Gray Lady activities at NIH since 1956.

Two NIH Scientists Named To New Posts

Two scientists have been appointed to new posts within NIH this month.

Dr. Elizabeth Frame has been appointed to the staff of the Center for Aging Research, DGMS. She transferred to her new post from the Clinical Center, where she was head of the Biochemistry Service, Clinical Pathology Department. Dr. Frame was commissioned in PHS in 1953.

Dr. Maurice Bender has been named executive secretary of the Cancer Chemotherapy Study Section. He was formerly a public health research program analyst in DGMS. Before coming to NIH last year he was a biochemist in the Fish and Wildlife Service, Department of the Interior; a faculty member at Rutgers University; and a pharmacologist at the U. S. Army Chemical Center.

NLM Drug Exhibit In CC

A new exhibit, "Psychopharmacology--Diet, Drugs for Men's Souls," is on display at the west end of the north corridor, third floor of the Clinical Center.

The exhibit, on loan from the National Library of Medicine, PHS, is sponsored by NIMH-NINDB Basic Research. It may be seen through July 31.

R&W NOTES

Mark Ellsworth, concertmaster of the National Gallery Orchestra, will direct the newly formed NIH symphony orchestra. Rehearsals will start in September, and, to date, 65 employee-musicians have expressed interest in the organization. Rosalie Silverberg, extension 4396, has more information.

Present R&W membership is now above 3,700.

Plans are now under way for the Hamsters' eighth "Life at NIH." The script committee has been meeting this month, and the presentation is planned for fall.

Dr. Miles Appointed Visiting Scientist

Dr. Albert E. W. Miles, professor of dental histology and pathology, London Hospital Medical College, England, has been appointed a visiting scientist in NIDR. During September and October he will participate in studies related to forensic dentistry.

Dr. Miles, known for his work on age-changes in calcified tissues, will engage in NIDR studies related to individual age determination by means of teeth.

JUNIOR OFFICERS CLUB ENDS AFTER 18 YEARS

The NIH Junior Officers Club, formed here in 1941, was officially disbanded last month by the club's executive committee. The committee voted to donate the group's assets to the PHS Officers' Wives Club.

A spokesman for the club pointed out that the organization's original functions--providing scientific seminars and regular meetings on medical subjects--are now being carried out by the Institutes and Divisions, so that the group's activity is no longer needed.

Emma S. Robinson Dies

Emma S. Robinson, 50, nursing assistant in the CC Nursing Department, died July 4 at Prince Georges General Hospital, Cheverly, Md., from injuries suffered in an automobile accident earlier that day.

A native of North Carolina, Mrs. Robinson came to NIH in 1957 after service as a student practical nurse at George Washington University Hospital and as a nurse's aide at Providence Hospital.

Mrs. Robinson lived at 4519 Kansas Ave., N.W.



Ben Goofin--lunches in unsafe places