

The NIH Record

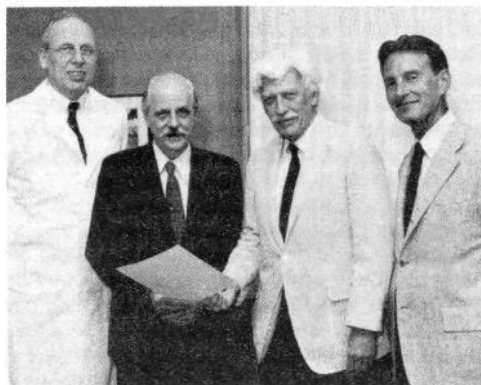
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Dr. Gilbert Ashwell Named First Institute Scholar at NIH

Dr. G. Gilbert Ashwell, former chief of the Laboratory of Biochemistry and Metabolism, National Institute of Arthritis Diabetes, and Digestive and Kidney Diseases, has been promoted to the rank of Institute Scholar. Dr. Ashwell is the first NIH scientist to be honored with this new rank.



Dr. Ashwell (second from l) is the first NIH scientist to be promoted to the rank of Institute Scholar. Standing with him are (l to r): Drs. Jesse Roth, director, NIADDK Division of Intramural Research; J.E. Rall, NIH Deputy Director for Intramural Research, and William B. Jakoby, Chief, Laboratory of Biochemistry and Metabolism, NIADDK.

The Institute Scholar rank was established this year by the Scientific Directors in order to provide a suitable honor for investigators of outstanding accomplishment. The intent is to free them from administrative burdens, and provide the environment with which to carry out their scholarly investigative activities.

This award is separate and distinct from the rank of Scientist Emeritus, which is awarded only to those scientists of high caliber who have retired. The Institute Scholar award is based on accomplishment alone, without regard to age of the honored investigator.

Dr. Ashwell started his NIH career at NIADDK (formerly NIAMD) in 1950 when he became involved in a program assessing the effects of radiation on biological systems. About the same time he started a series of investigations on the biochemistry of carbohydrates. These studies became the focal point of Dr. Ashwell's career.

(See DR. ASHWELL, Page 12)

Concentrated Calcium, Aluminum Imaged in Brains Of Parkinsonism-Dementia Victims for First Time

By Joyce McCarthy

Prominent concentrations of calcium and aluminum in brain tissue from Guamanian Chamorro patients with parkinsonism-dementia (PD) have been imaged for the first time by NIH scientists and reported in a recent issue of the *Proceedings of the National Academy of Sciences*.

Using computer-controlled electron beam X-ray microanalysis, the scientists found the distribution and produced images of calcium and aluminum in neurofibrillary tangle (NFT)-bearing neurons within the hippocampal region of the brain. The elemental images show the striking colocalization of both calcium and aluminum within the cell body and axonal process of the same NFT-bearing hippocampal neurons in this dementing disease. Deposits of calcium and aluminum were not found in non-NFT-bearing neurons in the hippocampus of the patients or controls.

In 1956, the National Institute of Neurological and Communicative Disorders and Stroke (then known as the National Institute of Neurological Diseases and Blindness) established a research station on the island of Guam to study the unusually high incidence of amyotrophic lateral sclerosis (ALS) and PD. Both disorders frequently occur within the same Chamorro families and occasionally in the same individual. They are chronically progressive and uniformly fatal and lead to death in 4 to 5 years.

Two other high incidence foci of ALS and PD have been documented in western Pacific populations. One occurs among Japanese living in two remote regions in the Kii Peninsula of Honshu Island and the other among the isolated Auyu and Jakai people living on the southern coastal plains of West New Guinea. In several West New Guinea villages,

(See PD VICTIMS, Page 10)

The Making of NIH Research Grants (I)

The NIH System for managing research grant applications may appear to be a huge bureaucratic maze, through which an application moves in a highly impersonal, lengthy and sometimes confusing manner. But the reality is far different.

This article—and a second article to follow—take the unfamiliar reader on a brief journey through the system that NIH uses for processing, reviewing, and deciding about awards on the thousands of research grant applications it receives every year.

Receipt, Processing, and Referral

Investigators use the PHS Form 398 application kit to submit research grant applications. This kit is available either at their organization's application control office or from the Office of Grants Inquiries in the NIH Division of Research Grants (DRG).

Applications must be sent to the DRG Referral Section, the central receiving point for most Public Health Service applications, by one of three annual dates listed in the application kit.

Once DRG receives the application, it is given a unique number, which refers to the type of application, the awarding unit of NIH to which it is assigned, and the grant support year. For example: 1 RO1 CA 12789-01A1

means the application is a new research project grant (RO1) application assigned to the National Cancer Institute (CA) with a serial number of 12789. The applicant is applying for a first year of support (01) and has already revised the application once (A1) in response to a previous NIH review.

Each application is assigned to an initial group for review of its scientific merit and to one or two bureaus, institutes, or divisions for a second review and possible funding. (The second article explains this "second review" in detail.)

Assignments are made by referral officers, who are professional health science administrators, most of whom also manage review groups.

Initial review group assignments are based on specific review guidelines of each committee; institute assignments (for second review) are based on the mission of the institute as well as its specific program, mandates and interests.

In FY 1983, DRG received and processed 24,660 Public Health Service applications. The vast majority of these—21,747 or approximately 88 percent—were reviewed by NIH.

(See NIH GRANTS, Page 11)

The NIH Record

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TRAINING TIPS

The following courses sponsored by the Division of Personnel Management are given in Bldg. 31.

<i>Executive, Management and Supervisory</i>	<i>Course Starts</i>	<i>Deadline</i>
The Federal Budget Process	9/17	8/31
<i>Technical</i>		
Proofreading	9/5	8/31
Medical Terminology I	9/11	8/21
Telephone Techniques	9/12	8/31
Effective English Workshop	10/15	10/1
Travel Orders & Vouchers	10/1	9/17
<i>Administrative</i>		
Files Maintenance & Disposal	9/10	8/20
Basic Time & Attendance Procedures	9/10	8/20
DELPRO (for new users only)	9/10	8/27
Computer Literacy		
A Hands-on Course (for GS 9-12)	9/25	9/11
(for GS 13 & above)	9/27	9/11
Using an Electronic Spreadsheet		
A Hands-on Course (GS 13 and above)	9/10	8/27
(GS 12's eligible on a space available basis)		

To learn more about these and other courses, contact the Development and Training Operations Branch, DPM, 496-6371.

CORRECTION

The Introduction to Extramural Programs (Sept. 10-11), is being offered through the Grants Associates Office, not by the STEP Program as stated in the *NIH Record*, July 31. For information on the program, you may call A. Robert Polcari or Roberta Light on 496-1736. □



On July 27 the National Library of Medicine honored eleven staff members and two other PHS employees who completed a six-course "Library Technology Program" sponsored by the NIH Career Education Center through the University of the District of Columbia. The program, presented during 1981-84, provided theoretical and technical training to support the specialized operations of the NLM and other government health-related libraries. The employees receiving certificates of completion are (from l to r): Juanita Williams, Carole Rodill, Mary Thomas, Marjorie Price, Katherine Vick, LaVerne Williams, Lucille Johnson, John Horne, Harriet Brooks, James Charuhas, Elsie Browne, Michael Daniel, Sylvia Bullock.

Medicine for the Layman Series Begins in September

The Clinical Center begins the 8th season of its Medicine for the Layman series on Sept. 11 with "You and Your Aging Parents," presented by Dr. T. Franklin Williams, Director, NIA.

In more than 60 lectures over the past 7 years, NIH scientists have shared their knowledge on such topics as heart attacks, cancer, obesity, stroke, influenza, epilepsy, and depression. The presentations are held on Tuesday evenings at 8 p.m. in Masur Auditorium through Nov. 20.

With the aid of colorful slides and films to make them understandable and entertaining, the lectures explore the latest research advances in health and disease.

Dr. Williams' lecture will address the stresses of age and its effect on the children of older people. Along with providing guidelines on coping, the discussion will explode some of the myths associated with aging.

It will be followed by "Child Psychiatry: Modern Approaches," presented by Dr. Judith Rapaport, chief, Child Psychiatry Branch, NIMH, on Sept. 25; "New Treatments

in Ophthalmology," by Dr. Carl Kupfer, Director, NEI, on Oct. 2; "Arthritis Today," by Dr. Paul Plotz, chief, section on connective tissue diseases, Arthritis and Rheumatism Branch, NIADDK, on Oct. 9; and "Hearing Impairment: The Invisible Handicap," by Dr. Ralph Naunton, director, Communicative Disorders Program, NINCDS, on Oct. 16.

On Oct. 23, the series will continue with "Aspects of Alcoholism," by Dr. Markku Linnola, clinical director, National Institute on Alcohol Abuse and Alcoholism; "AIDS: Acquired Immune Deficiency Syndrome," by Dr. Anthony Fauci, chief, Laboratory of Immunoregulation, NIAID, on Oct. 30; "Parkinson's Disease: Natural and Drug-Induced Causes," by Dr. Irwin Kopin, director, Intramural Research Program, NINCDS, on Nov. 13; and "Sleep and Its Disorders," by Dr. Wallace Mendelson, chief, unit on sleep studies, Clinical Psychology Branch, NIMH, on Nov. 20.

For further information on the series, contact the Office of Clinical Reports and Inquiries at 496-2563. □

Arylawn Accepts Fall Applications

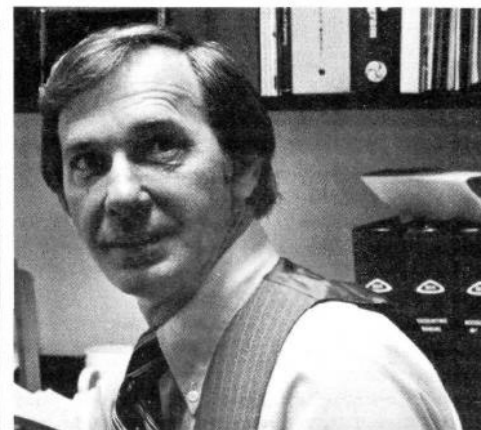
Parents of Preschoolers, Inc. a nonprofit parent-run corporation, is now accepting applications at the Arylawn Child Care Center, located close to the NIH campus, for its fall enrollment.

POPI operates a kindergarten program in conjunction with the Montgomery County public schools, as well as a Before-and-After School Program for children up to 12-years-old.

The center is open 5 days a week, Monday through Friday from 7:30 a.m. to 6 p.m. The program provides care in the mornings before school, at noontime for kindergarten only and after school hours. There is a full day program during school holidays and Christmas and Easter vacations.

The Arylawn program has a diversified staff of teachers and teacher aides. Staff/child ratio is 1:13.

For further information contact Anne Schmitz, 530-5550. □



Robert C. Patrick recently joined NIEHS as budget officer where he will be responsible for financial management of an annual budget that was more than 179 million dollars in fiscal year 1984. Previously, he worked in NIH's Central Budget Office in Bethesda.

NIH Gets MetroRail Service on August 26; Red Line Will Open as Far as Rockville

MetroRail held an open house at NIH Aug. 1 showing off Medical Center station, part of the newest link in the northern extension of the Red Line.

Service officially begins Sunday, Aug. 26, but free train rides will be offered Aug. 25 from Tenleytown, to Friendship Hts., to Bethesda, and Medical Center, ending at Grosvenor station in Rockville.

4th Largest

The Medical Center station, located on the corner of South Dr. and Rockville Pike across from Bethesda Naval Hospital, has the 4th largest escalator ride in the MetroRail system. It lasts 1 minute, 44 seconds. Wiley Powell, head of MetroRail's general maintenance and custodial service, said, "If you think that's long, the Bethesda station escalator will be at least twice as long."

Ride-On bus service is currently serving commuters in North and East Bethesda residential areas to supplement existing transportation to the Bethesda, Medical Center, and Grosvenor stations. Buses are running every ½-hour from 6:15 a.m. to 7 p.m. and cost 60¢ with a 10¢ transfer charge to another Ride-On bus.

In January 1985, Ride-On bus service and Metrobus routes will be modified to complement MetroRail service for the entire line which opens to Shady Grove station in December.

MetroRail hours are 6 a.m. to midnight Monday through Friday; 8 a.m. to midnight Saturday, and from 10 a.m. to 6 p.m. Sunday.

Bike-on-Rail

NIHers interested in taking their bicycles on MetroRail are required to have a Bike-on-Rail permit. To obtain a permit, you must make an appointment to take a mini-class on rules and regulations for MetroRail bike safety, pass a test, and pay \$15 for a 5-year permit with your picture on it.

Classes are given every Wednesday and Friday at 2 p.m. (limited to eight people), and on Saturdays at 11:30 a.m. (limited to 15 people), at the Metro Bldg., 600 5th St., N.W., Washington, D.C. Bicycles are allowed on MetroRail, in the last car, all day on holidays (except July 4), weekends, and after 7 p.m. during the week. Call 637-1116 for more information on bicycle permits.

Police Patrol

A Kiss-and-Ride parking area is located across from the Medical Center station and there are some metered parking spaces. The Montgomery County Police Department has requested that NIH employees be advised that beginning Aug. 25, the Kiss and Ride restrictions in the parking area at the Medical Center Metro Station, located on the east portion of the NIH campus, will be enforced by the Montgomery County Police.

The Montgomery County Police will also be



Everything is in working order for the Aug. 25 opening of MetroRail's northern extension of the Red Line. Trains are currently doing practice runs throughout the five new stops.



MetroRail's maintenance workers are putting finishing touches on the Medical Center station. They were polishing the chrome escalator during the Aug. 1 open house.

patrolling the flow of traffic on Wisconsin Ave. and South Dr. in the vicinity of the Medical Center Metro Station. In addition, there will be no NIH parking lots converted to MetroRail parking spaces in the future. □

Photos by Bill Branson



Ride-On buses are providing supplemental commuter service to MetroRail throughout the Bethesda area.



Elijah Steptoe, 8, from Upper Marlboro, Md., enjoys the escalator ride with his teacher and fellow patients from 3 East in the Clinical Center.

Food for a Healthy Heart: Campaign Results Reported

Can eye-catching posters, nutrition bulletins, and radio spots attract grocery shoppers to buy better foods for a healthy heart?

A pilot nutrition education program titled *Foods for Health*, conducted by an unusual partnership between the National Heart, Lung, and Blood Institute and Giant Food Inc., a major food retailer, has provided some interesting answers to this question. The answers appear in a 219-page report describing and evaluating the 1-year program.

Foods for Health: Report of the Pilot Program notes that nutrition information can be communicated successfully in the supermarket where food-purchasing decisions are made. While the program's impact on food-buying habits and food awareness was mixed, *Foods for Health* was well received by consumers and has generated broad interest among other organizations that have decided to adopt the program.

The program sent the following message to consumers: Given the facts, "you decide" whether to change your eating habits. During the study period, Giant Food distributed nutrition information in 90 of their Washington, D.C. area stores, mainly through *Eaters' Almanacs*, short, highly illustrated brochures updated every 2 weeks.

The *Almanacs* tried to increase awareness of the best foods to eat for a healthy heart—those lower in saturated fats, cholesterol, calories, and salt—and offered recipes and practical buying and menu tips for making dietary changes. Baltimore area Giant Food stores served as a comparison group and did not receive any written materials or media promotion.

The campaign staff circulated over 2 million *Eaters' Almanacs* and communicated to consumers through shelf signs, banners, posters, and radio and newspaper ads.

Evaluators of the campaign then surveyed 2,400 people via telephone. Customers returned 6,500 *Almanac* questionnaires and 2,200 shopper comment cards.

Total sales data was collected for 18 food categories using computer checkout classifications. The evaluators analyzed week-to-week sales fluctuations in nine categories: chicken, cottage cheese, margarine, milk, yogurt, and oils, as well as beef, eggs, and salt.

While no statistical difference in food-buying trends was found between the total number of consumers in the Baltimore and the Washington area stores, over two-thirds of those who responded to an *Eaters' Almanac* questionnaire said that reading the *Almanac* helped them decide to change their diets. Ninety-five percent of these respondents who changed their diets, and 75 percent of those who did not, said the information helped them maintain good eating habits.

Both men and women found the information helpful, although men to a somewhat greater degree (72 percent compared to 65 percent for women). Additionally, by the program's end, shoppers in the Washington area demonstrated an increased knowledge about nutrition for a healthy heart, whereas shoppers in the Baltimore area did not.

Over 15,000 inquiries about the program were received during the year-long campaign, and an additional 4 million *Eaters' Almanacs* were later distributed by Giant Foods. The program has since been adopted by health maintenance organizations, supermarkets, businesses, and schools. Nine million *Almanacs* have been circulated within Army commissaries worldwide, and Exxon Chemicals is using them in their headquarters' cafeteria.

Single copies of *Foods for Health: Report of the Pilot Program*, and updated copies of the *Eaters' Almanacs* may be obtained by writing to: Public Inquiries and Reports Branch/HL; National Heart, Lung, and Blood Institute, Bldg. 31, Rm. 4A21; Bethesda, MD 20205; or telephone (301) 496-1766. □



At the NIGMS annual awards ceremony recently, 30 employees and one former employee received honors. Patricia S. Jordan, budget analyst, (c), received the NIH Award of Merit from Dr. Ruth L. Kirschstein, NIGMS Director, (r), as her supervisor, Guy E. Hodgkins, financial management officer, looks on. Also receiving the NIH Award of Merit (not shown) were: Evelyn Laten, secretary, biophysics and physiological sciences program; and Marian A. Park, formerly a supervisory grants assistant in the NIGMS Office of Program Activities (OPA) and now a grants management specialist in NIA. Ten employees (not shown) received superior work performance awards: Carolyn M. Baum, program assistant, OD; Pat Clark, grants clerk, cellular and molecular basis of disease program; Rossie I. Fitzgerald, supervisory grants technical assistant, OPA; Beverly Hines, lead grants technical assistant, Office of Review Activities; Linda Huss, secretary, Office of Research Reports; Margie Otts, grants fiscal assistant, OPA; Marie Perrell, supervisory grants technical assistant, OPA; and Chuck Willoughby, grants fiscal assistant, OPA. Awards for special acts or services were given to (not shown) Annette Gage, grants technical assistant, Office of Review Activities; and Diane Moxley, personnel management specialist, Personnel Office. Eighteen employees were recognized for the length of their government service.

Visiting Scientist Program Participants

Sponsored by Fogarty International Center

6/26 **Dr. Ida Silvestri**, Italy. Sponsor: Dr. Hiroshi Taniuchi, Laboratory of Chemical Biology, NIADDK, Bg. 10, Rm. 9N313.

7/1 **Dr. Oscar R. Colamonici**, Uruguay. Sponsor: Dr. Leonard M. Neckers, Laboratory of Pathology, NCI, Bg. 10, Rm. 2N110.

7/1 **Dr. Shoju Hiraga**, Japan. Sponsor: Dr. Ronald G. Blasberg, Nuclear Medicine Dept., CC, Bg. 10, Rm. 1C401.

7/1 **Dr. Teruyuki Kimura**, Japan. Sponsor: Dr. Ida S. Owens, Laboratory of Developmental Pharmacology, NICHD, Bg. 10, Rm. 6C211.

7/1 **Dr. Toshikazu Kigoshi**, Japan. Sponsor: Dr. Kevin J. Catt, Endocrinology and Reproduction Research Branch, NICHD, Bg. 10, Rm. 8C404.

7/1 **Dr. Kazuo Kumami**, Japan. Sponsor: Dr. Maria Spatz, Laboratory of Neuropathology and Neuroanatomical Sciences, NINCDS, Bg. 36, Rm. 4B22.

7/1 **Dr. Michael A. R. Magerstadt**, Germany. Sponsor: Dr. Otto A. Gasnow, Radiation Oncology Branch, NCI, Bg. 10, Rm. B3B69.

7/1 **Dr. David W. McChesney**, U.S. Sponsor: Dr. Henry Metzger, Arthritis and Rheumatism Branch, NIADDK, Bg. 10, Rm. 9N240.

7/1 **Dr. Kentaro Mori**, Japan. Sponsor: Dr. Louis Sokoloff, Laboratory of Cerebral Metabolism, NIMH, Bg. 36, Rm. 1A27.

7/1 **Dr. Kevin D. Mullen**, Ireland. Sponsor: Dr. E. Anthony Jones, Digestive Diseases Branch, NIADDK, Bg. 10, Rm. 4D52.

7/1 **Dr. Moshe Z. Papa**, Israel. Sponsor: Dr. Steven A. Rosenberg, Surgery Branch, NCI, Bg. 10, Rm. 2B44.

7/1 **Dr. Simon Plummer**, United Kingdom. Sponsor: Dr. Curtis Harris, Laboratory of Human Carcinogenesis, NCI, Bg. 37, Rm. 2C07.

7/1 **Dr. Johannes Rosel**, Germany. Sponsor: Dr. Bernard Moss, Laboratory of Viral Diseases, NIAID, Bg. 5, Rm. 316.

7/1 **Dr. Eitan Shiloni**, Israel. Sponsor: Dr. Steven A. Rosenberg, Surgery Branch, NCI, Bg. 10, Rm. 2B44.

7/1 **Dr. Andre Veillette**, Canada. Sponsor: Dr. Robert C. Young, Laboratory of Medicinal Chemistry and Biology, NCI, Bg. 10, Rm. 12N226.

7/1 **Dr. Dag E. von Lubitz**, Denmark. Sponsor: Dr. Igor Klatzo, Laboratory of Neuropathology and Neuroanatomical Sciences, NINCDS, Bg. 36, Rm. 4D04.

7/2 **Dr. Tsuneyoshi Horigome**, Japan. Sponsor: Dr. Kenneth S. Korach, Laboratory of Reproductive and Developmental Toxicology, NIEHS, Research Triangle Park, N.C.

7/8 **Dr. Eduardo Charreau**, Argentina. Sponsor: Dr. Maria Dufau, Endocrinology and Reproductive Research Branch, NICHD, Bg. 10, Rm. 8C408.

7/8 **Dr. Mitsuo Honda**, Japan. Sponsor: Dr. Ethan Shevach, Laboratory of Immunology, NIAID, Bg. 10, Rm. 11N312.

7/8 **Dr. Mao Jiangsen**, China. Sponsor: Dr. Stephen Feinstone, Laboratory of Infectious Diseases, NIAID, Bg. 7, Rm. 210.

7/8 **Dr. Linda Koo**, Hong Kong. Sponsor: Dr. William J. Blot, Environmental Epidemiology Branch, NCI, Landow, Rm. C307.

7/8 **Dr. Ira Kurtz**, Canada. Sponsor: Dr. Maurice Burg, Laboratory of Kidney and Electrolyte Metabolism, NIADDK, Bg. 10, Rm. 6N307.

7/8 **Dr. Abraham Levy**, Israel. Sponsor: Dr. Joseph M. Rifkind, Laboratory of Cellular and Molecular Biology, NIA, GRC, Baltimore, MD.

7/8 **Dr. Myra A. Lipses**, Canada. Sponsor: Dr. Arthur S. Levine, Developmental Endocrinology Branch, NICHD, Bg. 10, Rm. 10B09.

7/8 **Dr. Pierre Tambourin**, France. Sponsor: Dr. Douglas R. Lowy, Laboratory of Cellular Oncology, NCI, Bg. 37, Rm. 1B19.

Skin Test to Detect Genetic Predisposition To Manic Depression Reported by Scientists

A test that detects and may predict genetic vulnerability to manic-depressive illness and related mood disorders in children has been developed by scientists from the National Institute of Mental Health.

Affective mood disorders afflict up to 15 million Americans with one-quarter of the U.S. population suffering from major serious depression costing \$10 billion annually. Such severe, persistent, months-long depression is characterized by decreased appetite, sex drive, social activity, hope, and lessened self-image with 15 percent of cases ending in suicide.

Since environmental factors play a role in such affective (emotional) illness, the test—which is based on a sample of skin cells (fibroblasts)—cannot predict with certainty who will develop the illness. But if its validity is confirmed in future studies, the test may—for the first time—enable doctors to identify individuals at risk because they carry predisposing genes. It should spur research into a disorder which has until now eluded efforts to establish a genetic marker.

Drs. N. Suzan Nadi, John Nurnberger and Elliot Gershon of the NIMH Intramural Research Program reported their findings in the July 26 *New England Journal of Medicine*.

Manic-depressive patients and their relatives with a history of affective disorder were found to have more receptors for acetylcholine—a chemical messenger regulating mood, memory, sleep and other aspects of brain function—in their skin cells than their never-depressed relatives and normal controls.

In addition, women were found to have more receptors and afflicted with more major depressive mood disorders than men, possibly indicating an increased genetic susceptibility and vulnerability to the illness.

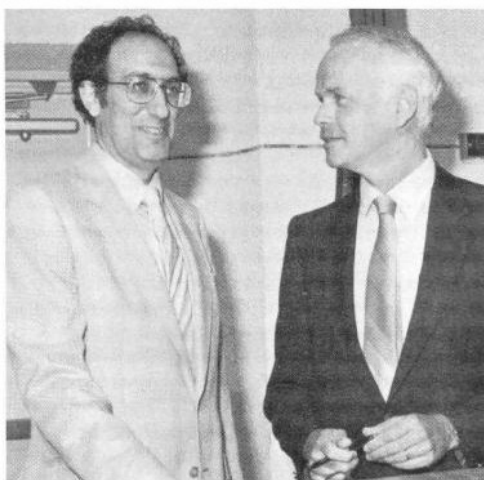
While the familial/genetic transmission of manic-depressive illness and other major affective disorders is well established, the mechanisms by which the inherited vulnerability finds expression are just beginning to be understood.

Studies show that an individual with one affectively ill parent runs a 27 percent risk of developing a mood disorder; the risk increases to 74 percent when both parents have a history of such illness.

The NIMH investigators had reason to suspect that the chemical/receptor system in the brain for the neurotransmitter acetylcholine plays a role in this process because of certain reactions exhibited in manic-depressive patients when given drugs that enhance, work against, or block acetylcholine.

In lieu of brain cells, the NIMH research team established a bank of skin cells from patients, their relatives and normal subjects. These cells contain some of the same chemicals and receptors as brain cells because they share a common evolutionary origin although the brain cells have become more specialized. When grown in laboratory test tube cultures, the cell lines reproduce rapidly, compressing a generation into about 1 week's growing time.

The scientists discovered that after growing the fibroblasts in test tubes for several



Drs. Gershon (l) and Goodwin answered many reporters' questions during the recent NIMH press briefing on their recent study of genetic markers for depression.

generations, cells from the 18 patients and 13 relatives who had histories of affective disorder generally showed a higher density of receptor binding sites than 5 normal relatives or 12 unrelated normal controls.

However, this association did not hold true for all families. A bipolar (manic-depressive) woman whose receptor density is the lowest among the patients, has a manic-depressive son whose son's cell line contains the lowest receptor count seen in ill relatives.

The scientists found:

- Drugs that enhance the neurotransmitter's activity worsen depressive symptoms and some that work against acetylcholine appear to lift depressions;
- Tricyclic antidepressant drugs block acetylcholine receptors;
- A drug that inhibits the enzyme that breaks down acetylcholine relieves manic symptoms.

One of the acetylcholine enhancers, arecoline, induced REM (rapid eye movement) sleep more rapidly among bipolar (both manic and depressive) depressed patients in remission than among normals in a series of NIMH studies.

Since REM sleep onset is known to be regulated by the acetylcholine system, the latter finding suggested that such patients may have supersensitive brain acetylcholine systems even when not depressed—possibly due to increased receptors. In effect, this cholinergic supersensitivity might be the genetically transmitted trait which predisposes such individuals toward having depressions and manias.

In relatives of the manic-depressive patients with increased receptors, a variety of mood disorders has been found, including schizoaffective disorder, manic-depressive illness, unipolar (major depressive) disorders and others. Again, these relatives have increased cholinergic receptor density.

Studies show that a child of bipolar parent actually runs a slightly higher risk of developing unipolar depression than manic-depressive illness; similarly, a child of a schizo-affective parent carries a higher risk

First Internat'l Workshop On Neuroimmunomodulation Slated

The First International Neuroimmunomodulation Workshop, devoted to discussing how the nervous, immune, and endocrine systems interact, will be held November 27-30, 1984, in NLM's Lister Hill Auditorium at NIH.

The workshop is designed to promote free and open exchange of data and ideas, to encourage ongoing and new research, and to provide opportunities for increased collaborative research in neuroimmunomodulation.

Among the speakers will be Nobel laureates, heads of research institutes and laboratories, and young, active investigators from many nations.

The workshop's sponsors include the National Institute of Neurological and Communicative Disorders, the National Cancer Institute, the Office of Naval Research, and Hoffmann-La Roche, Inc.

Registration for the workshop is extremely limited due to space restrictions. For more information, contact Dr. Novera Herbert Spector, Fundamental Neurosciences Program, NINCDS, Federal Bldg., Rm. 916, Bethesda, Md. 20205; telephone (301) 496-5745. □

Depression Study Needs Patients

NIMH psychiatrists are currently seeking patients with depression for an ongoing study of the possible biological bases of this illness. Patients will be studied as inpatients for 2 to 4 weeks and the tests will include a wide variety of blood tests and a spinal tap (optional, but desirable) as well as a complete medical and neurological evaluation.

Applicants must be referred by a personal physician or psychiatrist. Prior to entering this study, patients must be off all medications for at least 2 weeks; in some cases this may be accomplished during the hospitalization.

After completion of the study, patients will be returned to the care of their private doctors, who will be sent a complete report of the findings as well as a statement regarding the possible implications for diagnosis or treatment.

Referral is by physicians only. Personal physicians of interested applicants should call Dr. Owen Wolkowitz or Dr. Alec Roy at 496-6295. □

for both unipolar (depression only) and bipolar illness than for schizo-affective disorder.

"We want to emphasize that the disease is not just biological, however. We think that people inherit a vulnerability to it, and psychological and social stress sets off that vulnerability," said Dr. Frederick Goodwin, director of the NIMH Intramural Research Program.

Dr. Gershon added that in the future, two-thirds of all manic depression may be redefined as increased receptor disorder. He said that if the test proves valid, it could accurately detect children who have inherited a tendency to manic depression and allow early treatment because often the illness begins there but looks like other diseases such as alcohol abuse, drug abuse or antisocial behavior. —J.M. □

Disaster Medical Assistance Team at Work



John Nazario, chief of the Clinical Center's Materiel Handling Department, gives pointers on how to lug a stretcher.



Acquiring fake wounds is a young woman participating in the government-sponsored mock disaster at Andrews AFB. A team of artists from Walter Reed Army Medical Center applied moulage—phony wounds—to casualties.

NIH volunteers to the Disaster Medical Assistance Team, part of a newly organized National Disaster Medical System, practiced caring for and evacuating casualties during a mock disaster drill held recently at Andrews Air Force Base. Some 20 NIHers are part of a PHS contingent that will exemplify the kinds of skills needed in case of a disaster.

Representatives of 17 Federal agencies and the military are currently organizing a system for providing quick, quality medical care to victims both at the disaster site and at hospitals around the nation.

For a week, teams composed of local PHS employees practiced handling 125 patients a day at Andrews, sending some to hospitals by bus, others by helicopter.

In September, the 30 or so NIH employees who practiced at Andrews will receive more intensive training at Fort A. P. Hill in Virginia. □



NIH volunteers (from left) John Nazario, Dr. Floyd Brinley and Corwin Strong pause during drill to discuss strategy.



Casualties will be cleared from the scene of a disaster by helicopter or ambulance-buses.

Type II Diabetes Subject Of Recent "Teach-In"

The American Diabetes Association sponsored a recent nationwide diabetes "teach-in" aimed at educating a broad group of physicians on the diagnosis and treatment of type II (noninsulin dependent) diabetes.

The event was part of the ADA's ongoing effort to "Find the 5 Million" people who are estimated to have diabetes without knowing it.

Health professionals attended symposia in 27 locations across the country, the highlight of which was a panel discussion by experts in New York relayed by satellite simultaneously to each local gathering.

Drs. Phillip Gordon (in St. Louis) and Simon Taylor (in Washington) from the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases' intramural diabetes clinical program were panel members. Many NIADDK grantees sat on local panels, and the national panel included three current principal investigators on NIADDK grants.

An estimated 1,600 health professionals attended the Washington, D.C., locations for the symposium; the Twin Bridges Marriott and the Sheraton-Washington hotels. An estimated 20,000 to 30,000 health professionals attended across the country.

Type II diabetes affects about 80 percent of the estimated 11 million people in this country who have diabetes. About half of these individuals don't know they have the disease because type II diabetes can be present without causing symptoms that would send the person to the doctor.

Type I diabetes, in contrast, requires insulin injections and is rapidly fatal without treatment.

Type II diabetes—which generally begins later in life and is often called maturity onset diabetes—poses special problems in detection and treatment. Because symptoms can be subtle, identifying the disease may depend on the alertness of the physician to signs of diabetes and skill in carrying on and interpreting diagnostic tests.

Detection and adequate control of this type of diabetes is needed to prevent and manage long-term complications of diabetes that can develop even when the disease itself is not apparent.

These complications include cardiovascular disease which is much more common in diabetics; eye and kidney disease; and neurological problems that can lead to, for example, persistent sores on the feet and legs.

Control of type II diabetes can be difficult, and physicians—including the experts—do not agree on a number of therapeutic issues. □

VOLUNTEERS

R&W is looking for volunteers to work in the R&W office or Activities Desk.

Those applying can work Mondays, Fridays, or both days from 9 a.m. to 3 p.m.

If you or someone you know would like to assist with fund raisers, activity programs or day-to-day operations, call Randy Schools or Dotty Pulver at 496-6061. □

Scientific Coordinator for Environmental Cancer Dr. Herman F. Kraybill Retires After 40 Years

Dr. Herman F. Kraybill scientific coordinator for environmental cancer, Division of Cancer Etiology, NCI, retired August 3 after 14 years with the Institute and 40 years service with the Federal Government.

Dr. Kraybill first joined NCI in 1961 as assistant director for field studies and worked on emerging areas of environmental carcinogenesis, with special emphasis on mycotoxins, food degradation products, and food additives identified as carcinogens.

Dr. Kraybill left NCI from 1963 to 1972 to become chief of the pesticide program, Bureau of States Services, PHS, and then assistant director for biological sciences, Bureau of Science and Bureau of Foods, FDA.

When he returned to NCI in 1972, he initiated the interagency collaborative group on environmental carcinogenesis, a research coordination program involving 28 federal agencies. As chairman and NCI representative on the group, he worked with the established interagency working groups on environmental and occupational cancer.

He was instrumental in fostering the exchange of scientific information among agencies and drew attention to the significance of carcinogens in air, water, food additives, drugs, cosmetics, and workplace exposures. He emphasized the importance of multiple exposures in the carcinogenic process.

He received the NIH Award of Merit for his work in environmental cancer in 1981. He has published over 150 papers, contributed chapters to books, and is editor or coauthor of four books on toxicology and carcinogenesis.

Prior to first joining NCI, Dr. Kraybill served with several other federal agencies as a biochemist, toxicologist, nutritionist, and radiobiologist in such fields as human and animal nutrition, radiological health, radiation applications, and public health aspects of pesticides.

He considers his experiences in biomedical research at the U.S. Army medical research and nutrition laboratory, Fitzsimmons Army Hospital in Denver, Colorado, re-



Dr. Kraybill

warding. There, he gained national and international recognition for his research and direction of a national program on the nutritional value and safety of radiation-processed foods.

In addition to government service, Dr. Kraybill also worked in industrial research and development for 5 years. He served as nutrition consultant in the army medical department in World War II, and has held teaching appointments in chemistry and biochemistry at the University of Colorado, University of Denver, and University of Maryland.

Dr. Kraybill was born in Pennsylvania and received his B.S. in chemistry from Franklin and Marshall College, Lancaster, Pa. The college awarded him the Distinguished Alumnus Award in 1976. He earned his M.S. in physical chemistry in 1938 and his Ph.D. in biochemistry in 1941 from the University of Maryland.

After retiring, he will do consulting work with local foundations and academia. He will also pursue his interests in genealogy and Mennonite history, stamp and coin collecting, and travel, and most of all, the University of Maryland's athletic programs and marching band. □

Professor Yajima Rejoins FIC As Scholar-in-Residence

Professor Haruaki Yajima is returning for his third term as a Fogarty Scholar. He was educated at Kyoto University in Japan where he majored in organic chemistry and minored in pharmacology. He received his Ph.D. degree in 1956 and then went to the University of Pittsburgh to study peptide synthesis with Professor Klaus Hoffman in the department of biochemistry.

During the 6 years he spent with Prof. Hoffman, he was the key person in the team responsible for the first synthesis of an active ACTH molecule, and published more than 30 scientific papers.

He returned to Japan in 1962 to teach at Kyoto University. Since then, he has achieved the total synthesis of human ACTH and a number of other important hormonally active peptides, including motilin, substance P-cholecystokinin and pancreozymin and a

spectacular synthesis of ribonuclease A with full activity.

One of the most eminent synthetic peptide chemists in the world, Prof. Yajima has received many honors.

While he is at NIH, he will be associated with the Laboratory of Chemical Biology, NIADDK; the Laboratory of Developmental and Molecular Immunity, NICHD; and the Division of Biochemistry and Biophysics, NCDB.

Dr. Yajima's office will be located in Stone House, and he may be reached on 496-1213. □

The true teacher defends his pupils against his own personal influence.—Bronson Alcott

That man is richest whose pleasures are cheapest.—Thoreau

Vitamin D Metabolite May Curb Bone Disease

High doses of the Vitamin D metabolite, calcitriol, may be effective as an alternative, or supplemental therapy for bone marrow transplants in curbing the malignant bone disease, osteopetrosis, according to recent research by two NIADDK grantees.

"Osteopetrosis" refers to a rare hereditary disease characterized by abnormally dense bone. In the severe recessive or malignant form, which affects infants, diffuse overgrowth of bone effaces the marrow cavities and passageways of the cranial nerves in the skull, resulting in anemia and blindness.

In normal skeletal turnover or remodeling, there is a balance between bone formation and resorption. In osteopetrosis, however, bones become very dense because of faulty resorption, possibly due to impairment of bone-removing cells called "osteoclasts."

Because osteoclasts are believed to be derived from precursor cells in the bone marrow, marrow transplantation has been the only accepted treatment for osteopetrosis. However, this procedure carries serious risks, such as graft-vs-host reactions, and a suitable transplant donor is not always available.

A recently published article in the *New England Journal of Medicine* indicates that high-dose therapy with the vitamin D metabolite calcitriol (1,25 dihydroxy vitamin D) may be an alternative or addition to marrow transplantation for osteopetrosis.

An afflicted 8-week-old infant was given gradually increased doses of calcitriol over a 3-month period. A variety of tests showed increased bone turnover in the infant compared to 9 control subjects. In addition, the electron microscope revealed osteoclasts with ruffled borders, indicating activation of these bone-resorbing cells. Bone resorption remained normal for 6 months after treatment was discontinued.

Results show that very large doses of oral calcitriol improved bone resorption in a patient with congenital osteopetrosis. Although this encouraging effect was not mirrored by X-ray changes or significant clinical improvement, the evidence does indicate beneficial mobilization of bone mineral and matrix.

NIADDK grantees Drs. Mirjke Holtrop and Lyndon Key at Children's Hospital Medical Center (Boston), and collaborators supported by other NIH Institutes through Harvard Medical School (Boston), Washington University School of Medicine (St. Louis), and the Jewish Hospital of St. Louis, reported their findings in the recent issue of the *New England Journal of Medicine*. □

Baseball Tickets

R&W has scheduled two trips to Baltimore Orioles games for \$12.50 which includes bus transportation and game tickets.

The two games are: Friday, Sept. 7—Orioles vs. Milwaukee, upper reserved seats; Friday, Sept. 21—Orioles vs. Boston Red Sox, upper box seats.

The bus will leave from Bldg. 31C at 5:30 p.m. sharp. Sign up now at the R&W Activities Desk, Bldg. 31 or the Westwood R&W Gift Shop, Rm. 10. □

NCI Scientists Search for Secrets of Why Some Cancer Cells Develop Drug Resistance

By Steven I. Benowitz

During the last 20 years, cancer researchers have made great strides in finding drugs that are effective against a variety of cancers. In most cases, patients with diseases once considered incurable—such as Hodgkin's disease and childhood leukemia—can now be successfully treated with the help of powerful anticancer drugs.

But scientists admit that chemotherapy—treatment with anticancer drugs—still has a long road ahead. Drugs used in such treatments are aimed at the rapidly dividing cancer cells, but may damage normal cells as well. As a result, some types of chemotherapy may produce life-threatening effects on normal, healthy tissues.

Another major roadblock to the successful treatment of many cancers is the sudden development of resistance to the drugs being used to eliminate the cancers. A drug that has reduced the formation of cancer cells or reduced the size of a cancerous tumor may become ineffective, and the patient may relapse—the cancer cells may start to reproduce again. Cancer cells often find ways to avoid a drug's effects, and "turn off" its anticancer activity, rendering it ineffective. When cancer cells become drug-resistant, other strategies must be tried.

Doctors usually try to overwhelm the resistant cancer cells by introducing new drugs, or new combinations of drugs. But the cancer cells are often able to resist these new agents as well—even drugs they haven't encountered before, drugs that have different structures and mechanisms of action.

At a recent National Cancer Institute combined clinical staff conference, several NCI scientists described new and promising approaches that are helping doctors to better understand the underlying mechanisms of drug resistance, and devise ways to overcome it.

According to Dr. Greg Curt of NCI's Division of Cancer Treatment, drug resistance can take one of two forms. For some cancers, chemotherapy may have little or no curative effect. These cancer cells are inherently, or naturally, resistant. With other cancers, a drug treatment may be very effective initially, eliminating much of the cancer. But then the cancer may develop, or acquire, resistance to the drug, and the drug may not work anymore. The cancer cells can then begin to grow again.

Many scientists have found that certain types of cancers stop responding to chemotherapy because mutant cells, already present in the cancer cell population, are drug-resistant. These drug-resistant cells then become the forebearers of a new population of cells insensitive to the drug.

According to a new mathematical model developed by Canadian scientists the larger the cancerous tumor, the more likely it is to have resistant cells present. As a result, some patients may already have resistant cancer cells before they walk through the doctor's door.

Such a model, said Dr. Ken Cowan, a senior staff fellow in NCI's Clinical Pharmacology

Branch, would call for the use of combinations of drugs early in chemotherapy—and alternating the drugs—since the risk of developing resistant cells to two or more drugs is less than developing resistance to a single drug. Such techniques have had some success, notably in the treatment of advanced Hodgkin's disease and testicular cancer.

In some cases, resistance develops only to one or two chemically similar drugs, permitting the use of others that attack cancer cells in a different way.

The anticancer drug methotrexate, for example, works by binding very tightly to a certain cellular enzyme, Dr. Curt said. The enzyme is deactivated, and cancer cell division is prevented. But to be most effective, methotrexate must be metabolized—chemically converted in the cell—to slightly different forms, called "polyglutamates."

One form of resistance to methotrexate appears to be caused by a decrease in this type of drug metabolism. In small-cell lung cancer, using cells grown in the laboratory in the presence of methotrexate, Dr. Curt has found that as these cells become drug-resistant, fewer and fewer polyglutamates are formed inside the cell. At the same time, through genetic changes called gene amplification, cancer cells "learn" to produce large amounts of the enzyme that is deactivated by the drug, overriding the drug's therapeutic effectiveness, and allowing the cancer to grow again.

Researchers are now seeking ways to overcome another roadblock in which resistance develops simultaneously to a whole series of different drugs. According to Dr. Bruce Chabner, director of NCI's Division of Cancer Treatment, this type of resistance may indicate that the cancer cell membrane has changed in a way that enables it to either block drug entry into the cell, or permit the rapid diffusion of the drug from the cell, after it has entered. In any event, the time the active drug remains inside the cell is reduced.

Dr. Chabner has noted that some cancer cells show increased amounts of a certain protein on the cell membrane, noticeable only when a cancer is resistant to a drug treatment; this protein may influence the way a drug enters or leaves the cancer cell. For certain cancers, the protein "marker" could become a target at which to aim specific "killer antibodies."

Changes at the cancer cell membrane may be implicated in the development of drug resistance in patients with ovarian cancer. Dr. Robert F. Ozols, senior investigator in NCI's Medicine Branch, believes drug resistance is the number-one cause of treatment failure in such patients. In ovarian cancer cells grown in the laboratory, Dr. Ozols has shown that some drug-resistant cells may let a drug enter, only to push it out before it can exert any anticancer effect.

Dr. Ozols and others have found that a class of drugs called calcium channel blockers, commonly used to treat heart problems, can sometimes overcome this "pushing-out" effect and make cancer cells sensitive to cer-

tain anticancer drugs. It appears that calcium channel blockers overcome resistance by blocking the mechanism responsible for the increased efflux of drugs from resistant cells, Dr. Ozols said. Clinical trials are already under way to see if these drugs, when combined with other anticancer agents, are useful in the treatment of ovarian cancer.

Researchers have found ways to overcome drug resistance in cells grown in the laboratory, Dr. Cowan said. Several of these approaches are now being used with some success on patients in clinical trials. These include alternative ways of administering drugs, such as injecting the drug directly into a region like the abdomen, in order to increase the local concentration of drug delivered to a cancer site. □



NICHD's Women's Organization, the oldest continually active women's group at NIH, recently celebrated its 10th anniversary. Since its inception in May 1974, the organization has served the Institute's employees by organizing career development and health enhancement seminars. Shown holding the birthday cake are (l to r): Jane Showacre, former chair; Myrtle Coleman, secretary; Rayna Blake, Federal Women's Program manager; Hildegard Topper, chair; Barbara Witkin and Peggy Garner, former chairs. □

Attn: CEC Transition Participants Planning To Attend UDC in Fall

Are you a former Career Education Center (CEC) participant? Are you eligible for the CEC Transition Program as described in the CEC Transition brochure and the orientations held last April? If so, you'll want to take note of the following information.

- Guidelines for completing HHS Form 350 have been mailed to all current CEC participants;
 - Program policy will be mailed to current CEC participants within the next two weeks.
 - University of District of Columbia (UDC) registration dates, on the UDC campus, by last name initials are:

Aug. 20	A-D
Aug. 21	R-Z
Aug. 22	E-J
Aug. 23	K-Q
Aug. 24	For students who missed their registration date.
 - A representative from the UDC Registrar's Office will be on the NIH campus to discuss registration procedures Aug. 15, 1984 at 11 a.m.
- If you have a question about your eligibility or did not receive a copy of the guidelines, please call Edith Pruden on 496-6211. □

Pregnant Smokers Who Stop Can Improve Birth Weight

Pregnant smokers who cut back or stop smoking during pregnancy can improve the birth weight of their newborns, according to a new study supported by NICHD.

This is the first known randomized clinical trial to show that an antismoking program initiated during pregnancy favorably affects the birth weight of the infant. The study of 935 pregnant smokers was conducted by Dr. Mary Sexton and Dr. J. Richard Hebel at the University of Maryland School of Medicine.

The investigators used an assistance program designed to help the women stop or reduce their smoking during pregnancy.

Women who were not more than 18 weeks pregnant and smoked at least 10 cigarettes a day were asked to participate in the study and randomly assigned to one of two groups.

In the treatment intervention group, trained counselors provided the women with assistance, information and guidance to stop smoking. A similar group of pregnant smokers, who did not receive any anti-smoking assistance, served as the control group.

Biochemical Test Used

A comparison of the two groups showed that infants born to the mothers receiving antismoking information were an average 92 grams (0.20 lbs.) heavier and 0.6 cm (0.24 inches) longer than infants born to the control group mothers.

Both groups of women were contacted during the 8th month of pregnancy to obtain information on their smoking habits before delivery.

The percentage of women quitting smoking by the 8th month of pregnancy was two times greater in the group receiving antismoking counseling than in the control group.

The researchers also used a biochemical test, thiocyanate levels in the saliva, to more accurately measure the number of cigarettes smoked by the participants. The results of this test showed significantly higher levels of the cigarette chemical in the control group compared to the group receiving antismoking assistance.

Although the difference in weight between the infants born to both groups is not large, it does show the negative effect of maternal smoking on fetal growth. Numerous studies have confirmed that women who smoke during pregnancy have infants whose birth weights average 200 grams (0.44 lbs.) less than infants born to women who did not smoke.

More recently, studies have been focusing on the mechanisms by which the substances in cigarette smoke adversely affect the growth of the fetus.

Ingested cigarette smoke, containing tar, nicotine, carbon monoxide and other toxic substances, circulate through the mother's blood and crosses the placenta into the fetal tissue. Some researchers suggest that the carbon monoxide may interfere with the delivery of oxygen to the fetus—an essential element for fetal growth and development.

This study was reported in the *Journal of the American Medical Association*, Vol. 251, No. 7. □

More than 100 Presidents and Administrators Of Minority Colleges Attend EA Workshop

More than 100 presidents and science administrators from black, minority and women's colleges and universities across the country attended the second national NIH Extramural Associates (EA) Program Workshop held recently on the NIH campus. Attendance of the EA Institution presidents was an unprecedented occasion.

The theme of the workshop was "Entering the Age of Science and Technology: The Role of EA Institutions."

NIH Director Dr. James B. Wyngaarden welcomed the participants.

The workshop attracted high interest in bringing institution presidents and associates together to develop strategies for expanding research activities, programs and science initiatives now and in the future. Costs of the workshop were shared by participating institutions with NIH.

Since its inception in 1978, the Extramural Associates Program has established close working relationships between NIH and 68 black, minority and women's colleges and universities in 26 states and in Puerto Rico.

In his welcoming remarks, Dr. Wyngaarden expressed his support and told the participants, "I regard these developing ties between your institutions and the National Institutes of Health as an important part of NIH progress toward broadening the family of grantees and expanding the opportunities for investigator-initiated research."

The purpose of the program, which continues to expand, is to encourage and broaden the research capabilities and participation of EA Institutions in national biomedical research through equal access to extramural programs and funding both within and outside of NIH.

The workshop was attended by 150 participants including 53 institution presidents or their designees and 55 extramural associates. The associates spend 5 months in residence at NIH learning about research policies and procedures in order to provide leadership and place new emphasis upon the development of research activities at their respective institutions upon completion of their residency.



The keynote address at the EA workshop was delivered by Dr. Thomas Malone, NIH Deputy Director. To Dr. Malone's right is Dr. John Diggs, director, NIAID Extramural Activities Program.

NIH Deputy Director, Dr. Thomas E. Malone, delivered the keynote address, "Facing the Challenge of Change." Dr. Malone said, in part: "The participation of EA Institutions in these years of scientific progress has been limited because of a history that needs no reiteration here. The history simply imposes an awesome burden of entry on you. But this is why NIH initiated, in the early 1970s, programs designed to redress the inequities of the past and to embrace a vast potential that has literally been scorned for the nation's scientific effort."

The workshop included eight work groups led by NIH staff members in discussing EA institution commitment, the use of institution faculty and resources, the pursuit of funding opportunities and methods and procedures for expanding research activities. Each work group presented a report of their proposed strategies to the general assembly.

A 3-member panel of associates highlighted institution experiences in the development of research programs, and an associate introduced each of the four topics, followed by questions, prior to the work group discussions.

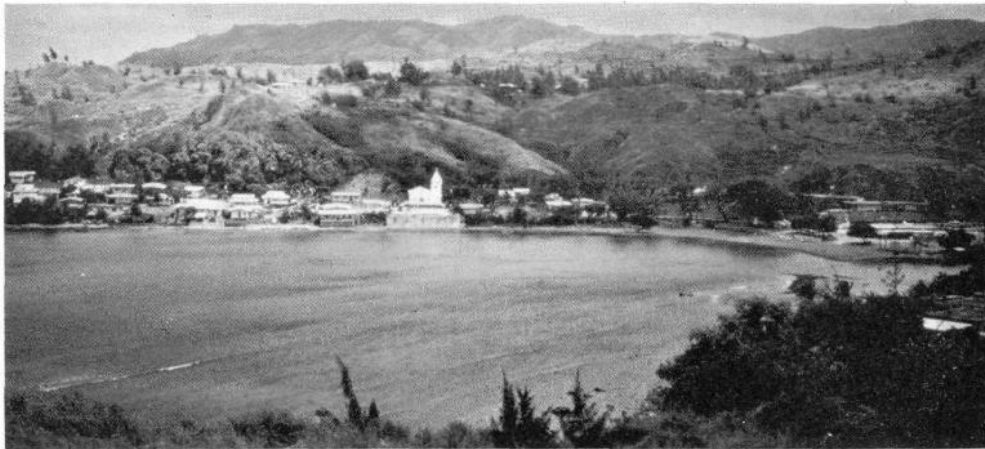
NIH Deputy Director for Extramural Research and Training, Dr. William F. Raub, also addressed the workshop. Participants were given a full tour of the NIH Clinical Center. □



During a Clinical Center tour, Dr. Alan Zabell, chief, radiation therapy section, Radiation Oncology, NCI, talks with EA workshop participants (from l to r): Drs. Jeanmarie DeChant, Notre Dame College of Ohio; Mary Finlay, Benedict College; Sr. Claire Markham, St. Joseph; partially hidden, Dr. William Kahl, Russell Sage; Drs. Julio Rivera and Carmen Mercado, Catholic University of Puerto Rico; Dr. Annette Bower, Mount St. Mary's; Dr. C. T. Enus Wright, Cheyney University; Dr. Warren Ashe, Howard University; unidentified NIH staff member; Dr. Louis Bone, Benedict; and Dr. Tossie Taylor, Cheyney University.

PD VICTIMS

(Continued from Page 1)



The village of Umatac, Guam, site of the highest incidence rates of ALS and PD on the island. In 1521, Magellan landed in Umatac Bay and claimed the island for Spain.

lages, ALS incidence rates approach nearly a thousand times the rate found in the continental United States.

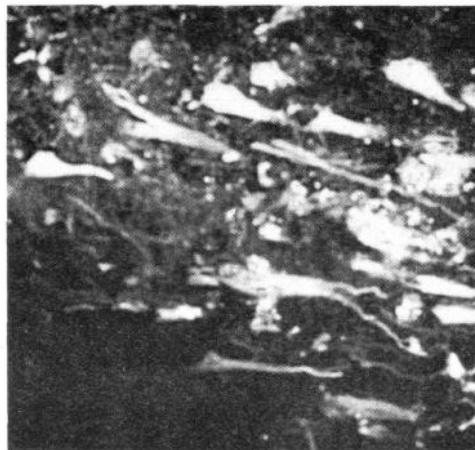
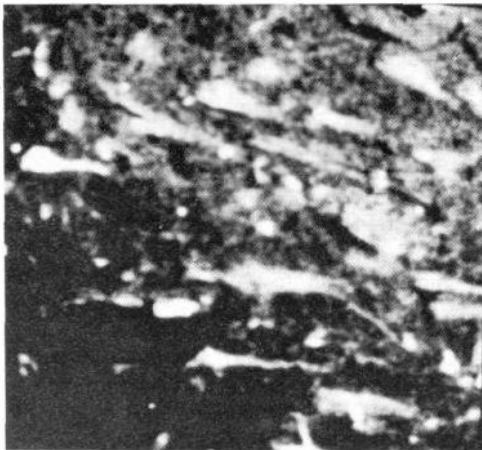
ALS, known as *lytico* on Guam, affects the motor neurons of the brain and spinal cord, resulting in progressive weakness, atrophy, and eventual paralysis and death. The disease affects thousands of individuals each year worldwide. PD, locally referred to on Guam as *bodig*, results in slowness of motor activity, disturbances in gait, rigidity, tremor and severe dementia.

Twenty-five years ago, more than 20 per-

cent of the native adult population of Guam died of these disorders. Since then, however, there has been a marked decline in incidence of ALS and PD, suggesting that environmental, rather than genetic, factors are etiologically important in these diseases.

Similar declines are also evident in the Kii Peninsula focus in Japan and, more recently, in two West New Guinea villages where Western contact and new foodstuffs have been introduced. In all three foci, severe deficiencies of calcium and magnesium and high concentrations of other metals, such as aluminum, have been found in garden soil and drinking water. In addition, subtle disturbances in calcium and vitamin D metabolism in ALS and PD patients and cortical bone loss in Guamanian children and adults have been demonstrated.

These findings support the hypothesis that defects in mineral metabolism and secondary hyperparathyroidism, provoked by chronic deficiencies of calcium and magnesium, have led to increased intestinal absorption of toxic metals and deposition of calcium and aluminum in central nervous system tissues of these patients.



Elemental images of the pyramidal cell layer of the hippocampus from a patient with parkinsonism-dementia of Guam showing the prominent accumulation of calcium (a) and aluminum (b) in NFT-bearing neurons from the same field. The images were generated using a new application of wavelength dispersive spectrometry and computer-controlled electron-beam X-ray microanalysis. The "brightest" cells in the images indicate areas of highest elemental concentration. The full field width of each picture is $\frac{1}{4}$ of a millimeter (or 250 micrometers).

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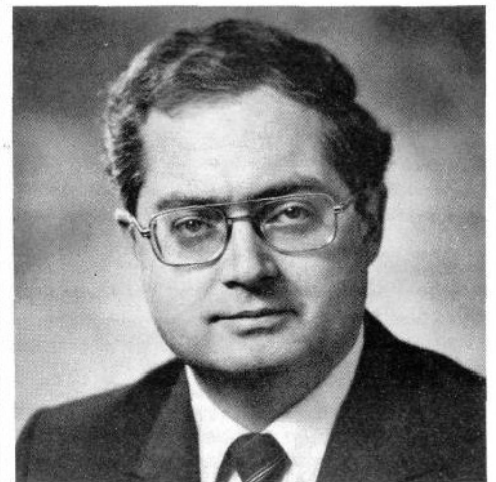
The current research was conducted at NIH in the Laboratory of Central Nervous System Studies, NINCDS; the Department of Clinical Pathology, Clinical Center; and the Biomedical Engineering and Instrumentation Branch by Drs. Ralph M. Garruto, Ryo Fakatsu, Richard Yanagihara, D. Carleton Gajdusek, Gregory Hook, and Charles E. Fiori and Keith Gorlen. Colleagues of the Computer Systems Laboratory, Division of Computer Resources and Technology, designed and assembled the sophisticated computerized automation and software used in the study. □

Fertility/Pregnancy Expert Dr. Gary Hodgen Leaves

Dr. Gary D. Hodgen, a fertility and pregnancy research expert, was recently named scientific director of the Institute for Reproductive Medicine at Eastern Virginia Medical School in Norfolk. Previously, he had been with the National Institute of Child Health and Human Development since 1969.

Serving as chief of NICHD's Pregnancy Research Branch, Dr. Hodgen came to national prominence through several significant research advances. His pioneering work in primates has led to new procedures in women.

In his new post, Dr. Hodgen will direct a major research program involving basic and clinical research. His long-range interests include plans to study the feasibility of gene therapy in embryos with the ultimate aim of preventing birth defects.



Dr. Hodgen

Last year Dr. Hodgen received the first President's Scientific Achievement Award of the Society for Gynecologic Investigation (SGI). He was cited as a "devoted, young investigator who has distinguished himself with a productive and diverse research career."

In addition, the SGI cited him for training more than 20 postdoctoral fellows, in both basic and clinical research, and for his service on the editorial boards of numerous journals.

Dr. Hodgen earned his doctorate in physiology from Ohio State University. □

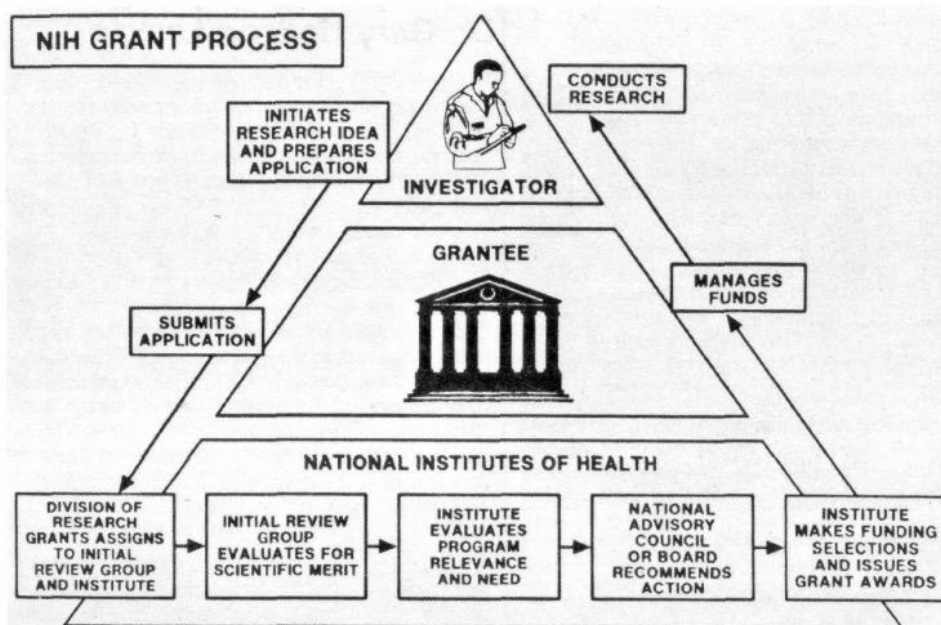
Research Reporter Wins Prizes

The Health Sciences Communication Association (HeSCA) has awarded the *Research Resources Reporter* of the Division of Research Resources the second and third prizes at their national competition.

Called "Print Festival '84," the contest honored the September and July 1983 issues of the publication.

HeSCA, founded in 1965, serves as a professional focal point for those engaged in health sciences communications, enabling them to share and exchange new concepts in the field.

The *Reporter* has received 24 awards for communications excellence in the last 5 years. □



Initial Group Review

In the NIH system of peer review, each application undergoes two levels of review. At the first level, panels of experts selected according to scientific disciplines or current research areas, evaluate the *scientific merit* of applications. These legally mandated panels, generally referred to as initial review groups, are called study sections in DRG.

Each initial review group of about 18 members is managed by an executive secretary, who is a health scientist administrator, assisted by a grants technical assistant.

The executive secretary nominates members and selects any needed ad hoc reviewers from the group of active and productive researchers in the biomedical scientific community. Regular members are appointed for up to 4 years and are staggered so that about a fourth of the group's members are new each year.

The main requirement for service is demonstrated scientific expertise. Other criteria include mature judgement, balanced perspective, objectivity, ability to work in a group, expressed interest in serving, personal integrity to assure confidentiality of applications and discussions, and adequate representation of women and ethnic minority

scientists.

Well in advance of a meeting, the executive secretary sends each member copies of all the applications to be reviewed at that meeting. Each application is assigned to two or three members, according to their expertise, for in-depth, detailed evaluations. Besides preparing these evaluations, each member is expected to read and become familiar with all the applications so as to participate in discussions at review meetings.

Initial review groups meet three times a year for 2 or 3 days each time, depending upon the number and types of applications received. DRG study sections, which are generally responsible for the review of research grant applications, normally review between 75 and 100 applications.

Institute review groups, which are usually responsible for the review of special-purpose and multidisciplinary applications such as those for program projects and centers, review fewer applications at each meeting because of the complexity of these applications.

During meetings, the assigned reviewers lead discussion of the applications on which they have prepared written critiques. Each

application is discussed individually according to specific review criteria, under the leadership of one member, who has been designated the chairperson by the executive secretary. The executive secretary provides policy and procedural guidance.

Mandated PHS review criteria on any proposed research include: (1) scientific, technical, or medical significance and originality; (2) appropriateness and adequacy of the experimental approach and methods to be used; (3) qualifications and experience of the principal investigator and staff in the area of the proposed research; (4) reasonable availability of necessary resources; (5) reasonableness of the proposed budget and duration of the research; and (6) the adequacy of means proposed to protect against adverse affects upon humans, animals or the environment (where such are involved).

For other types of grant applications, the review criteria vary according to specific requirements and objectives.

Voting Procedure

After discussion, each application is acted upon by majority vote. The vote recommends approval, disapproval, or deferral. Approval means that, based on the review criteria, the group believes the application merits support. Disapproval means the application is not of sufficient worth to merit support or involves gravely hazardous or unethical procedures.

Deferral means that the group cannot make a recommendation without more information. Such information can be obtained during a project site visit or from additional materials requested from the applicant.

On every recommendation to approve a grant application, each reviewer privately records a numerical rating of the scientific merit of the application. This rating is based on a scale from 1.0—the most meritorious—to 5.0, the least acceptable, using increments of 0.2.

After the meeting, the executive secretary averages the ratings for each application and multiplies by 100 to obtain a three-digit number known as the priority score. Priority scores guide the institutes in recommending the funding order for applications.—**Samuel H. Joseloff** □

S and T Parking Permit Names Must Be Renewed in September

General parking permits for NIH employees whose last name begins with S or T must be renewed during September.

Employees may renew their parking permits any workday at the NIH Commuter Assistance Office, Bldg. 31, Rm. B1C19, between 8:30 a.m. and 3:30 p.m. Parking permits will also be available as follows: Blair Bldg., Wednesday, Sept. 12, 1–2 p.m., Conf. Rm. 110; Federal Bldg., Wednesday, Sept. 19, 1–2 p.m., Conf. Rm. B119; Landow Bldg., Wednesday, Sept. 19, 2:30–3:30 p.m., Conf. Rm. C; Westwood Bldg., Wednesday, Sept. 12, 9–11 a.m., Conf. Rm. 3.

Affected employees will receive a memo reminding them of the upcoming renewal and providing specific instructions on obtaining replacement permits.

Employees with preferential (red) or carpool parking permits whose last name begins with S or T do not need to obtain new parking permits during September.

New September general employee parking permits must be displayed beginning Monday, Oct. 1. □

God made Man in his own image and then Man returned the favor—*Voltaire*

Body Fat Test

Body fat percentage can be easily determined by skinfold measurement, and the NIH Fitness Center in Bldg. T-39 will offer this service free Aug. 16 and 21 between 11 a.m. and noon.

Ideal body fat percentage for males is 16 per cent or less; for females, 23 per cent or less. Marginal obesity for males is 20 per cent fat and 30 per cent fat for females. Obesity is related to a higher incidence of such diseases as coronary heart disease, diabetes, cirrhosis of the liver, hernia and intestinal obstructions.

However, body fat can be reduced with proper exercise and nutrition. For information on exercise classes at noon and after work, call 496-TRIM. □

Dr. Margaret Dear Joins CC Nursing Staff



Dr. Dear

Dr. Margaret Dear has recently joined the Clinical Center Nursing Department staff as senior nurse scientist.

A social psychologist by training, Dr. Dear comes to NIH from Johns Hopkins University where she held faculty positions in both the School of Hygiene and Public Health and the School of Arts and Sciences. She was also director of nursing research at Johns Hopkins Hospital.

"I see my role as supporting nurses who are carrying out research projects," she said. "I also would like to encourage new research efforts, as well as continue carrying out my own research projects."

Dr. Dear said there is already a great deal of data and potential for projects in the Nursing Department.

"I'm quite pleased with the amount of research already going on within the department," she remarked. "We're in a very good position compared to other institutions."

Dr. Dear received her baccalaureate in nursing in 1956 from St. John's University, New York, and a masters degree in 1970 and Ph.D. in 1979 from Catholic University.

She has published extensively in nursing and behavioral science journals and texts, and has conducted funded nursing research.

She is a member of the Council of Nurse Researchers of the American Nurses' Association, Sigma Theta Tau, National Nursing Honor Society; and Alpha Kappa Delta, National Sociology Honor Society. □

Distinguished Scientist Award

The D.C. Chapter, Society for Experimental Biology and Medicine, is seeking nominations for the 1985 Award for Distinguished Scientist. The nominee need not be a member of the society. The awardee will be recognized in the fall of 1984 and will be asked to give a lecture in the spring of 1985.

Closing date for nominations is Sept. 1. For information call E. A. Brown after Aug. 13, at 447-8093. Send nominations to Dr. E. A. Brown, 6811 Nesbitt Place, McLean, Va. 22101. Include a letter summarizing the reasons for the nomination and a curriculum vitae of the nominee. □

DR. ASHWELL

(Continued from Page 1)

His contributions in carbohydrate biochemistry are numerous. Early studies include the discovery and preparation of xylulose 5-phosphate, providing the keystone for the pentose phosphate shunt.

Working with bacteria, Dr. Ashwell described mechanisms for the metabolism of an important group of sugars, the uronic acids. This class of sugars is biologically very important, and includes vitamin C.

His work with the role of sugars that are part of glycoproteins provided the first clue in answering the problems of how cells recognize these proteins. He discovered that removing one sugar, the end sialic acid, from a glycoprotein chain acted as a signal for removal of the glycoprotein and its destruction by the liver.

Subsequent work by Dr. Ashwell and others have now shown that the movement of glycoproteins from one site to another within the body, and from one site to another within single cells, is controlled by receptors which recognize specific sugar patterns.

Peer recognition led to Dr. Ashwell's election to the National Academy of Sciences in 1979, receipt of the Gairdner Foundation Award in 1982 and the Merck Award of The American Society of Biological Chemists in 1984.

Dr. Ashwell received his B.S. and M.S. degrees from the University of Illinois, and M.D. degree from Columbia University. He has served on the Board of Directors of the Foundation for the Advanced Education in the Sciences (FAES), on several committees of the American Society of Biological Chemists, and on the editorial boards of such journals as *Analytical Biochemistry*, *Archives of Biochemistry and Biophysics*, *Hepatology*, *The Journal of Biological Chemistry*, and the *Journal of Neurochemistry*. □

NIH Theater Group Holds Auditions for "Harvey"

The NIH R&W Theater Group will hold auditions for "Harvey," a comedy by Mary Chase, on Aug. 27 and 29 at 7:30 p.m. in the Masur Auditorium in Bldg. 10 (Clinical Center).

This play focuses on Elwood P. Dowd, a slightly absentminded middle-aged man who believes he has a six-foot (invisible) rabbit for a companion. Elwood's sister tries to have him declared insane, with surprising results.

Parts are open for six men aged 30 to 60 and six women aged 20 to 60. Technical, backstage, costume, house management and publicity assistants are also needed and are invited to attend the auditions. Show dates are scheduled for two weekends in mid-November.

For more information, call Sally Richardson at 598-5668. □

Malt does more than Milton can to justify the ways of God to man.—A. E. Houseman

Progress is the mother of problems.—G. K. Chesterton

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