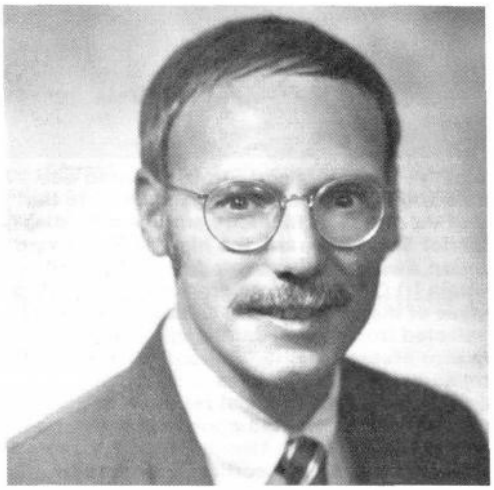
The NIH Record

U.S. Department of Health and Human Services

August 28 1984 Vol. XXXVI No. 18

National Institutes of Health

Dr. G. Khoury Will Present G. B. Mider Lecture



Dr. Khoury

Dr. George Khoury, chief of the Laboratory of Molecular Virology, NCI, will deliver the 1984 G. Burroughs Mider Lecture, "Enhancers—Regulatory Elements in Eukaryotic Gene Expression," at 8:15 p.m. Wednesday, Sept. 12, in the Clinical Center's Jack Masur Auditorium. The lecture is open to the public.

(See MIDER LECTURE, Page 8)

$10.5 Million Project

NIH and Howard Hughes Medical Institute Join to Train More Biomedical Researchers

The National Institutes of Health and the Howard Hughes Medical Institute are launching a multi-million dollar cooperative program to help increase the vigor of American biomedical research and continue the flow of new doctors into research careers, Health and Human Services Secretary Margaret M. Heckler announced on Aug. 16.

"When at full capacity, the new program will offer approximately 30 medical students a year, chosen competitively from the nation's medical schools, six months to one year of research training on the NIH campus in Bethesda, Md., under the guidance of leading NIH scientists," Secretary Heckler said.

"Many medical leaders perceive a shortfall in one important category of health research personnel: individuals who simultaneously have medical knowledge, clinical skills and scientific expertise," according to Dr. James B. Wyngaarden, NIH Director.

Dr. Donald S. Fredrickson, HHMI President and onetime NIH Director, said the joint project will enlarge the pool from which future physician researchers can be drawn.

HHMI, located in Coconut Grove, Fla., will support the program at a cost of approximately $10.5 million for the first 5 years. This will include stipends, travel and miscellaneous support for the students, as well as building renovation and construction for residential quarters, classrooms and teaching laboratories.

Dr. James B. Wyngaarden, Director of NIH, (r.) and Dr. Donald S. Frederickson, president of the Howard Hughes Medical Institute, sign an agreement under which HHMI will provide $10.5 million to house and train about 30 medical students in biomedical research at NIH for 5 years. A new wing (at left in architectural model) will house the students at what was a Convent of the Sisters of the Visitation. The present convent building is depicted at right in model.

HHMI will administer the program, and HHMI and NIH will cooperate on selection of students, counseling, teaching, and on continuing contact with students upon their return to their home institutions.

Recruitment will begin this fall with the first group of students entering the program in the fall of 1985. The center for the Hughes Research Scholars will be the Mary Woodard Lasker Center for Health Research and Education on the NIH campus, formerly a convent of the Sisters of the Visitation.

"It is expected that this early exposure to the excitement and intellectual challenge of research—after the second year of medical school—will encourage more medical students to undertake careers in biomedical re-

(See BIOMEDICAL PROJECT, Page 8)

Dr. John Seal, Eminent Scientist-Researcher In Infectious Diseases, Dies at Age 72

Dr. John R. Seal, 72, former Special Assistant to the NIH Director and former Deputy Director of the National Institute of Allergy and Infectious Diseases, died Saturday, Aug. 11, at the National Naval Medical Center following a long illness with cancer.

Dr. Seal conducted infectious disease research and administered research programs for more than 40 years, both as a medical officer in the U.S. Navy and as a NIH civilian employee.

Through the years, he played a pivotal role in directing research to control streptococcal infections, hepatitis, influenza, cholera, and other viral and bacterial diseases.

A native of Charleston, W. Va., Dr. Seal attended Davidson College in North Carolina, received his Doctor of Medicine from the University of Virginia School of Medicine, and interned at Strong Memorial Hospital in Rochester, N.Y.

(See DR. SEAL, Page 10)

Dr. John R. Seal

The NIH Record

Published biweekly at Bethesda, Md., by the Editorial Operations Branch, Division of Public Information, for the information of employees of the National Institutes of Health, Department of Health and Human Services, and circulated by request to writers and to researchers in biomedical and related fields. The content is reprintable without permission. Pictures may be available on request.

The NIH Record reserves the right to make corrections, changes, or deletions in submitted copy in conformity with the policies of the paper and HHS.

NIH Record Office
Bldg. 31, Room 2B-03, Phone 496-2125

Editor
Herschel Cribb

Staff Writers
Joyce F. McCarthy
Anne Barber

Editorial Assistant
Marilyn Berman

Staff Correspondents
CC, Richard McManus; DCRT, Joan P. Sobel; DPM, Harry Marshall; DRG, Sue Meadows; DRR, Barbara Menick; DRS, Jim Doherty; FIC, Susan P. Stark; NCI, Patricia A. Newman; NEI, Marsha Corbett; NHLBI, Larry Blaser; NIA, Marian Emr; NIAID, Jeanne Winnick; NIADDK, Barbara Weldon; NICHD, James Hadley; NIDR, Jody Dove; NIEHS, Hugh J. Lee; NIGMS, Wanda Warddell; NIMH, Harry Bell; NINCDS, Carol Rowan; NLM, Roger L. Gilkeson.

TRAINING

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

Executive, Management and Supervisory	*Course Starts*	*Deadline*
The Federal Budget Process	9/17	8/31
Technical		
Telephone Techniques	9/12	8/31
Effective English Workshop	10/15	10/1
Travel Orders & Vouchers	10/1	9/17
Secretarial Techniques	11/5	10/22
Administrative		
Files Maintenance & Disposal	To Be Announced	
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.

Retirement Planning Offered

The Recruitment and Employee Benefits Branch, Department of Personnel Management, is offering another Retirement Planning Program for NIH employees on Oct. 16 and 17.

A personnel bulletin will be distributed desk-to-desk giving more detailed information. □

The National Institute of Neurological and Communicative Disorders and Stroke honored outstanding scientists and support staff at the Institute's annual awards ceremony June 28 in the ACRF auditorium. William Weiss, (not shown) chief of the Office of Biometry and Field Studies (OBFS), received a Public Health Service (PHS) Superior Service Award, the highest PHS award for Civil Service employees. A PHS Special Recognition Award was presented to Dr. Richard Quarles, Intramural Research Program. Sylvia Edelstein (r) OBFS, was congratulated for having been named DHHS Outstanding Handicapped Employee of the Year. NINCDS Director Dr. Murray Goldstein pointed out that Ms. Edelstein had been selected from among candidates representing not just NIH but the entire Department. Dr. Goldstein also presented PHS Citations to Dr. Edward Ginns, "for outstanding research in the biochemistry and molecular genetics of the sphingolipidoses," and to Dr. Norman Barton, "for outstanding achievement in clinical research in the study of inherited disorders of metabolism." Dr. Goldstein also presented wooden plaques, honoring exceptional contributions to NIH, to six winners of the NIH Merit Award: Barbara Nichols, OBFS; Dr. Emanuel Stadlan, Demyelinating, Atrophic and Dementing Disorders Program; Dr. Maneth Gravelli, Anita Ley, Susan Titman, and Thelma Fletcher, all from IRP.

NIH Fitness Center Announces Fall Exercise Schedule

Registration for the NIH Fitness Center's fall exercise class begins Aug. 29 for the session starting Sept. 10.

Workout sessions continue through Dec. 15 (with exceptions as noted), with a makeup week of Dec. 17-22.

Fall Schedule

The fall exercise class schedule is:

Quik Fit (cardiovascular and total body workout)—Monday, Wednesday, Friday from noon to 12:45 p.m. and 5:15-6 p.m.; Monday and Wednesday from 6:05-6:50 p.m.

Alive! (ballet-like stretching, strengthening and body awareness)—Tuesday, Thursday from 11 a.m.-noon, 5-6 p.m. and 6-7 p.m.; Friday from 6:05-7:05 p.m.; Saturday from 9:15-10:15 a.m.

Beginning Fitness (very moderate exercises with gradual progression and fitness education)—Tuesday, Thursday from noon to 12:45 p.m. This class runs Oct. 9 to Nov. 15.

Pre- and Postnatal (Moderate stretching, strengthening, cardiovascular and relaxation exercises for pregnant or postpartum women.) Class dates are Sept. 24 to Oct. 29. Physician's consent is required.

Information and schedules may be picked up at the Fitness Center—Bldg. T-39 (phone: 496-TRIM), Activities Desk, Bldg. 31 (phone: 496-4600) and all R&W Gift Shops. □

WMTI Selectees Announced By Secretary Heckler

Fourteen NIH employees are among the 121 DHHS employees selected by DHHS Secretary Margaret Heckler to participate in the "Women's Management Training Initiative" (WMTI). Competition was keen, with over 1800 applicants evaluated.

In June of 1984, Secretary Heckler announced the initiation and implementation of a Department-wide "Women's Management Training Initiative". This program was designed to offer select supervisory and managerial training for high potential nonsupervisors in grades 9 through 12.

Applications were screened by a Departmental panel and final selections were made by the secretary. Persons selected for DHHS/WMTI will receive training during Fiscal Year 1985.

Orientation sessions and drafting of Individual Development Plans will begin in September.

Those NIH candidates selected to the WMTI are:

Lynda Bennett, NICHD; Marion Blevins, NIDR; Christine Chastain, NIEHS; Nancy Cherry, NHLBI; Sylvia Cunningham, NIAID; Patricia Gallahan, NCI; Alice Hines, NIA; Joann Holmes, OD; Dorothy Moore, NLM; Catherine Quigley, NLM; Linda Stalvey, NIADDK; Fu Sing Temple, NIGMS; Carol Watkins, NINCDS; Anne Zimmer, NIA. □

MetroRail

Discounts and Access for Handicapped Plus Parking and Bus Service Explained

Discount fares are available for the elderly and the handicapped riding MetroRail. Fares are half the prevailing rush or nonrush hour amounts with a maximum charge of 80¢. An above-ground elevator is located at the corner of South Dr. and Rockville Pike for those unable to use the Medical Center escalator.

Ride-On buses do not provide lifts for those in wheelchairs.

80¢ Minimum

MetroRail has a minimum charge of 80¢ and a maximum charge of $2.40; fares are based on the distance traveled. For instance, when Shady Grove station opens in mid-December, it will cost $1.75 during rush hour to ride to Medical Center or $1.10 during nonrush hour. The trip lasts 15 minutes.

Trips to Medical Center from Rockville will cost $1.40, lasting 11 minutes; from White Flint, 95¢, 9 minutes; and from Grosvenor, 80¢, 3 minutes. From Medical Center to Metro Center is $1.55, 19 minutes; $1 during nonrush hours.

Metro offers discount fares to the elderly and the handicapped.

Beginning Aug. 25 until mid-December, 900 free parking spaces will be open at the Shady Grove West parking lot for those interested in taking a Ride-On bus (for 60 cents) to the Grosvenor MetroRail station. Nonstop shuttle service will depart Shady Grove station every 15 minutes during rush hours.

Rush Hour Service

Rush hours are from 6 to 9 a.m. and from 4:30 to 7:30 p.m. This service is also available from the White Flint parking lot which has 931 free parking spaces; Ride-On shuttle service is available every 5 to 10 minutes from White Flint to Grosvenor.

When full operation of the northern extension of the Red Line to Shady Grove opens in mid-December, parking fees are projected to be $1 per day in the available parking lots at the different stations.

Grosvenor station has 580 spaces which will go fast during rush hour. Drivers will have to find some other place to park once those are filled and connect with Ride-On in other places. □

New Shuttle Bus Schedule Starts Sept. 4

Beginning Tuesday, Sept. 4, a new NIH Shuttle Bus schedule will go into effect. The new route/schedule will include the Medical Center Station and Parking Lot 41B, the only new stops. The shuttle buses will start their route at the Clinical Center and end at the Westwood Bldg. They will be operating at 20-minute intervals from 7:30 a.m. to 9 p.m., and will stop at their currently designated pick-up points, plus the two new stops noted above. (See accompanying schedule.)

			C ROUTE			
METRO DEPARTURE	BLDG. 31	BLDG. 10	BLDG. 36-37	BLDG. 12A	BLDG. 38A*	METRO
7:30 a.m.	7:34 a.m.	7:36 a.m.	7:39 a.m.	7:43 a.m.	7:46 a.m.	—
7:55 a.m.	7:59 a.m.	8:01 a.m.	8:04 a.m.	8:08 a.m.	8:11 a.m.	—
8:20 a.m.	8:24 a.m.	8:26 a.m.	8:29 a.m.	8:33 a.m.	8:36 a.m.	—
8:45 a.m.	8:49 a.m.	8:51 a.m.	8:54 a.m.	8:58 a.m.	9:02 a.m.	—
9:10 a.m.	9:14 a.m.	9:16 a.m.	9:19 a.m.	9:23 a.m.	9:26 a.m.	—
—	4:32 p.m.	4:34 p.m.	4:37 p.m.	4:41 p.m.	4:44 p.m.	4:47 p.m.
—	4:57 p.m.	4:59 p.m.	5:02 p.m.	5:06 p.m.	5:09 p.m.	5:12 p.m.
—	5:22 p.m.	5:24 p.m.	5:27 p.m.	5:31 p.m.	5:34 p.m.	5:37 p.m.
—	5:47 p.m.	5:49 p.m.	5:52 p.m.	5:56 p.m.	5:59 p.m.	6:02 p.m.

*Pickup at MLP-7A.

Enrollment Expanded Under Federal Health Program

Employees who lose coverage under a spouse's non-Federal health plan because the spouse was involuntarily separated as a result of a layoff from his/her employment may now enroll in one of the Federal health plans.

Under the same conditions, employees may also change from self to family enrollment. This eligibility exists within the period beginning 31 days before and ending 31 days after the spouse's employment terminates.

This new regulation became effective January 9, 1984.

Eligible employees may contact their BID personnel office to get details on this added opportunity to enroll under the Federal Employees Health Benefits Program. □

Wolf Trap's International Festival

Dancers in swirling, colorful skirts tapping out a Mexican beat, chants and dances from the heart of Africa and a folk country band playing a fiddle, harmonica and washboard. These are just some of the more than 100 performances and workshops scheduled for the 1984 International Children's Festival, scheduled for Sept. 1–3 at the Wolf Trap Farm Park in Vienna, Va.

Magicians, mimes, story tellers and others will choose children out of the audience to join in their performances. Although there will be concession stands, you may want to pack a picnic lunch.

Tickets may be purchased at the R&W Activities Desk, Bldg. 31, and the Westwood R&W Gift Shop, Rm. 10. Adults—$4; Children 4 and over $3. □

10-Mile Anniversary Run To Be Held Sept. 16

The 9th annual NIH Health's Angel anniversary 10-mile run will be held Sunday, Sept. 16, at 9:45 a.m.

As usual, the race will be cosponsored by the D.C. Road Runner's Club. For the first time, the race will be the 10-miler offered in the club's championship series.

DCRRC will provide trophies for the first three finishers in each of six age groups for men and women.

Ribbons Provided

The Health's Angels will again provide ribbons for all 10-mile runners and special awards for the fastest NIH man and woman, and the traditional "unbody" award to the fastest runner whose weight is 2.5 times or more his/her height in inches.

The race starts and finishes at the Kengar Recreation Center in Kensington and is run out-and-back on the well-shaded bike path along Beach Dr. with a short hill on Old Spring Rd. Peter Nye holds the course record of 52:12 for men, Patty Deuster set the woman's mark at 64:45. Jim Larkin has the best "unbody" time of 60:40.

The 10-miler will be preceded by a one-mile fun run for children 10 or under starting at 9 a.m. and a 2-mile "Run For Your Life" at 9:15 a.m.

All Events Open

All events are open to all comers. Registration will be on the day of the race with an entry fee of $1 (50¢ for DCRRC members). Last year's race, won by Robert Stack (54:44) and Amy Jermann (66:13), saw 125 runners of 128 starters finish with 60 finishers under 70 minutes. □

Conscience is the inner voice that warns us somebody may be looking.—H.L. Mencken

Diagnostic Criteria for Alzheimer's Disease Proposed by Broad Group of Scientists

By Emily Rudin

An interdisciplinary work group has proposed uniform criteria for collaborative therapeutic trials in Alzheimer's disease, and has recommended approaches for assessing the disorder's natural history.

The work group, jointly established by the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association, worked under the auspices of the DHHS Task Force on Alzheimer's Disease.

Published in *Neurology*, July 1984, the work group's report is the result of a comprehensive review of the requirements for diagnosing possible, probable, and definite Alzheimer's disease, a brain disorder marked by progressive dementia in middle or late life.

Such diagnostic standards are important for uniform comparison of research results among different institutions and nations, and for correlation of clinical diagnoses with pathological findings. The criteria will also help guide physicians in properly diagnosing and caring for Alzheimer's disease patients.

Highlights of the criteria include:

- The clinical diagnosis of *definite* Alzheimer's disease requires autopsy or biopsy confirmation of a clinical diagnosis of probable Alzheimer's disease.
- The clinical diagnosis of *probable* Alzheimer's disease is based on clinically determined dementia, confirmed by neuropsychological tests; two or more cognitive deficits; progressive worsening of memory and other cognitive functions; no disturbance of consciousness; onset between ages 40 and 90 (most often after age 65); and absence of systemic disorders or other brain disorders that could cause progressive deficits in memory and cognition.
- The clinical diagnosis of *possible* Alzheimer's disease should be used in research studies when a single, gradually progressive, severe cognitive deficit is identified in the absence of another cause.

"This project was a productive collaboration among scientists from Government, a voluntary health agency, and academic institutions," said Dr. Emanuel M. Stadlan, executive secretary of the work group and deputy director of NINCDS' Demyelinating, Atrophic, and Dementing Disorders Program.

The report was reviewed by six professional societies concerned with research and clinical care for Alzheimer's disease.

"With Alzheimer's disease," said Dr. Stadlan, "basic research from many different approaches is necessary before the etiology and pathogenesis are uncovered.

"I hope that an understanding of the disease, as enhanced by the contribution of this work group, will lead to ways to treat, prevent, or arrest the progression of this disorder," he said.

The group's participants were neurologists, psychiatrists, psychologists, pathologists, neuroradiologists, and other laboratory specialists.

Their affiliations included the NINCDS, Alzheimer's Disease and Related Disorders Association, National Institute on Aging, National Institute of Mental Health, and many medical centers and universities.

"The consensus of this work group is a significant step toward establishing an accurate base for research on Alzheimer's disease," Dr. Stadlan noted. "The need for generally agreed upon criteria has long been recognized.

"This wasn't the first attempt at developing criteria," he explained. "What our work group did was to identify criteria compatible with previous efforts, and to refine them so that 'possible' and 'probable' diagnoses could be made with some confidence. That neurologists, psychiatrists, and psychologists could agree upon and work with these criteria is significant."

Dr. Stadlan emphasized that there is still much to learn about Alzheimer's disease and that further refinement of these criteria will be inevitable.

"We still need to identify specific diagnostic markers of the disease," he said. "The development of more precise criteria is crucial, since a substantial number of cases diagnosed as Alzheimer's disease are discovered at autopsy to have had other diseases."

The report stresses the importance of encouraging those who treat demented patients to seek to identify possible reversible causes for the dementia. □

Visiting Scientist Program Participants

Sponsored by Fogarty International Center

7/8 **Dr. John Scott,** U.S. Sponsor: Dr. Bruce J. Baum, Patient Care Branch, NIDR, Bg. 10, Rm. 2B01.

7/8 **Dr. Joseph Zohar,** Israel. Sponsor: Dr. Dennis L. Murphy, Clinical Neuropharmacology Branch, NIMH, Bg. 10, Rm. 3D41.

7/9 **Dr. Alvar Gronberg,** Sweden. Sponsor: Dr. John Ortaldo, Biological Therapeutics Branch, NCI FCRF, Bg. 560.

7/9 **Dr. Paul Edwards,** Jamaica. Sponsor: Dr. Carl Kupfer, Ophthalmic Genetics and Pediatric Ophthalmology Section, NEI, Bg. 10, Rm. 10N226.

7/9 **Dr. Giovanni Salerno,** Italy. Sponsor: Dr. Edward G. Lakatta, Clinical Physiology Branch, NIA, GRC, Baltimore, MD.

7/10 **Dr. Jun-ichi Miyazaki,** Japan. Sponsor: Dr. Keiko Ozato, Laboratory of Developmental and Molecular Immunity, NICHD, Bg. 6, Rm. 1A03.

7/11 **Dr. Yoshihiro Furuki,** Japan. Sponsor: Dr. John W. Kebabian, Experimental Therapeutics Branch, NINCDS, Bg. 10B, Rm. 5C114.

7/11 **Dr. Ram Prashad Gupta,** India. Sponsor: Dr. G. E. Hook, Laboratory of Pulmonary Function and Toxicology, NIEHS, Research Triangle Park, NC.

7/11 **Dr. Ryuichi Konno,** Japan. Sponsor: Dr. Peter J. Wirth, Laboratory of Experimental Carcinogenesis, NCI, Bg. 37, Rm. 5C30.

7/11 **Dr. Susan Laurie, Canada.** Sponsor: Dr. E. F. Neufeld, Genetics and Biochemistry Branch, NIADDK, Bg. 10, Rm. 9D15.

7/13 **Dr. Jacov Tal,** Israel. Sponsor: Dr. Barrie Carter, Laboratory of Cell Biology and Genetics, NIADDK, Bg. 4, Rm. 316.

7/16 **Dr. S. Naim Ahmad,** India. Sponsor: Dr. Forrest Weight, Laboratory of Preclinical Studies, NIAAA, 12501 Washington Avenue, Rockville, MD.

7/16 **Dr. Mohamed H. Haddada,** France. Sponsor: Dr. Arthur S. Levine, Section on Viruses and Cellular Biology, NICHD, BG. 31, Rm. 2A50.

7/16 **Dr. Takao Yora,** Japan. Sponsor: Dr. Jacob Robbins, Clinical Endocrinology Branch, NIADDK, Bg. 10, Rm. 8N315.

7/17 **Dr. Peter Paul Muller,** Switzerland. Sponsor: Dr. Alan G. Hinnebusch, Laboratory of Molecular Genetics, NICHD, Bg. 6, Rm. 408.

7/17 **Dr. Kenji Tanimoto, Japan.** Sponsor: Dr. Thomas N. Chase, Experimental Therapeutics Branch, NINCDS, Bg. 10, Rm. 5C103.

7/18 **Dr. Jose Esteban, Spain.** Sponsor: Dr. David Colcher, Laboratory of Tumor Immunology and Biology, NCI, Bg. 10, Rm. 8B11.

7/18 **Dr. Rafick Sekaly, Canada.** Sponsor: Dr. Thomas Kindt, Laboratory of Immunogenetics, NIAID, Bg. 5, Rm. B104.

7/22 **Dr. Juan Bernar, Spain.** Sponsor: Dr. Michael A. Zasloff, Human Genetics Branch, NICHD, Bg. 10, Rm. 8C429.

James H. M. Austin Dies; In Radiation Safety 25 Years

James H.M. Austin, chief of the Radiation Support Section, Radiation Safety Branch, Division of Safety, died August 12 after a short illness. He was 52 years old and had been with the NIH Radiation Safety Program for over 25 years.

Mr. Austin joined NIH in 1959 as a physical science aide and rose to the position of chief, Radiation Support Section, where he had responsibilities for radioactive waste management and receiving and shipping of radioactive materials as well as operation of the "Hot Labs" in Building 21. He spent 4 years in the U.S. Air Force prior to joining NIH.

Jim Austin is remembered by his coworkers and by the NIH research community as a jovial person who was always willing to help with both routine and special problems relating to radioactive waste and radioactive materials shipments. He was an avid sports fan, especially Redskins football.

He is survived by his wife, Mable, a nurse in the Clinical Center, and two daughters, Sharon and Carolyn.

James H.M. Austin

Maryland Renaissance Festival

R&W will once again have tickets to the Maryland Renaissance Festival which begins on Aug. 25 and will run through Sept. 30.

R&W's tickets are discounted to $5; $2 off the regular $7 fee.

The Maryland Renaissance Festival is located at Symphony Woods adjacent to Merriweather Post Pavillion in Columbia, Md.

Pharmacological Whodunit: Tracing and Reducing Harmful Side Effects of Various Drugs

"No drug produces a single effect," states a pharmacology textbook by L.S. Goodman and A. Gilman. An important goal of pharmacologists—scientists who study the effects of biologically active compounds on living systems—is to help design drugs that have desirable therapeutic results with few adverse side effects.

Toxic reactions—which can range from unpleasant to fatal—are often caused by chemical changes made by the body in the process of metabolizing or breaking down a drug. Tracing the metabolic pathways taken by chemical substances is painstaking work for laboratory detectives.

There are frequently many pathways as well as many different metabolites (products of metabolism), some of which are both difficult to isolate and unstable, that must be investigated before the toxic culprit or culprits are cornered.

Dr. Sidney Nelson, a National Institute of General Medical Sciences grantee at the University of Washington in Seattle, is a pharmacologist studying metabolic pathways in several compounds, including acetaminophen and a mint-like flavoring agent called pennyroyal oil. Although it is usually a beneficial substance, acetaminophen (an ingredient in many non-aspirin-containing pain relievers and cold remedies such as Tylenol® and Datril®) can be toxic in huge doses.

Pennyroyal oil, which is sold in health-food stores for use in minute quantities to add flavor or fragrance, can cause fatal lung and liver damage in larger doses.

It is sometimes used by women attempting self-induced abortions, and although it is not clear how effective the oil is in achieving that result, its ability to cause death is well-documented.

Both acetaminophen and pennyroyal oil are metabolized in the liver by a process known as oxidation that involves the addition of oxygen atoms to the compound. A group of enzymes (substances that catalyze or speed up chemical reactions) called the cytochrome P-450s play a key role in the transformation by oxidation of these and other foreign substances.

Within therapeutic doses, acetaminophen is transformed by the P-450 system to a metabolite that is eliminated from the body without any adverse effects. Huge doses, however, overwhelm the usual protective mechanisms and the resulting sequence of events can lead to cell death.

Dr. Nelson's group has been able to successfully complete the difficult task of synthesizing for study a pure form of the highly toxic chemical N-acetyl-p-benzoacetaminophen. They are now studying NAPQI to learn how it is formed within a living organism and how it kills cells.

Like acetaminophen, certain components of pennyroyal oil are metabolized to toxic intermediate substances. Dr. Nelson and his group decided to isolate and examine these components, focusing on pulegone—a substance that constitutes 80 percent of the oil.

Interestingly, they found that pulegone shows stereo-selectivity—that is, it is composed of two structures, called enantiomers, which are mirror images of each other but cause markedly different toxic reactions. R-(+)-pulegone is much more toxic than its enantiomer, S-(−)-pulegone.

The researchers will now analyze the metabolic pathways of R-(+)-pulegone to investigate mechanisms by which the toxic metabolite or metabolites are formed.

Studies of this sort are important not only because they may lead to a possible treatment or antidote for a single substance, but also because they contribute to a general understanding of the mechanisms by which whole classes of toxic substances operate. Often relatively minor modifications to a chemical structure can alter metabolism and thereby modify toxicity.

The outcome of research like Dr. Nelson's can be the development of techniques that result in the synthesis of compounds that will not produce these undesired, and potentially serious, reactions.—**Doris Brody** □

Self-Defense, Not Attack, Is Keynote Of Tae Kwon Do as Taught at NIH

Tae kwon do is often called "Korean karate," and it does have some resemblance in style to karate.

However, it differs greatly from some other martial arts, according to Dr. W. French Anderson, chief of the Laboratory of Molecular Hematology in the National Heart, Lung and Blood Institute, and an expert in tae kwon do.

Dr. Anderson noted, for example, a basic difference between judo and tae kwon do. Judo is more of a wrestling, throwing sport whereas tae kwon do is like "boxing with the hands and feet," he said.

Since 1979, the NIH Tae Kwon Do Club has offered basic, intermediate and advanced training. Dr. Anderson founded the club and serves as its president.

"Ours is one of the larger American Athletic Union clubs in the country," he said. The membership at present is about 60 participants. Most of the students are NIH employees, Dr. Anderson said, but any R&W member can join.

Dr. Anderson said the club has a practically injury-free record—the most serious was a broken wrist when one student tripped and fell.

Although individual club members have competed in tournaments, the focus of the NIH organization is not on that aspect. "We orient much more around self defense and body control than fighting," he said.

For those who desire advanced competition-type instruction, the club maintains a "reciprocal relationship" with professional clubs in the area, so students can go to them for this purpose.

Dr. Anderson (background) works with two of the other black belt instructors in the NIH Tae Kwon Do Club, Mike Choi (l) and William Miller

In fact, members of the NIH club have no trouble blending in with mainstream clubs. "Our students have found that their technique is as good or better than schools around the country," Dr. Anderson said.

Another reason they find transition easy is the development in the last three years of the tae guek forms, a standardized set of moves. These were developed because tae kwon do will become an Olympic sport in the 1988 games and a more uniform set of moves was needed to replace the older ones which varied from place to place.

The tae guek forms became mandatory one-and-a-half years ago for clubs wishing to compete in the Olympics, Dr. Anderson said. Another requirement is membership in the American Athletic Union, to which the NIH club belongs.

Dr. Anderson also serves as team physician for the American national tae kwon do team, a job that he has held for 4 years. He became acquainted with the tae guek forms and switched the NIH club to them.

Dr. Anderson became interested in tae kwon do "purely as self-defense" in 1969, following the 1968 riots in Washington and trouble at NIH itself. Also during this time, he helped establish the NIH Police Force, and the club maintains a close relationship with them, he said.

Dr. Anderson now holds a third-degree black belt and acts as an instructor for the NIH club. Three other black belt instructors are associated with the organization: Mike Choi, an NHLBI summer research assistant; Dr. Daniel Eskinazi of the Laboratory of Oral Medicine, NIDR, William Miller of the Office of the Director, NIA.

These instructors hold 1- to 6-week clinics for various specialized areas of tae kwon do on Wednesay and Friday nights. Monday nights are devoted to regular instruction at the basic, intermediate and advanced levels.

Another offshoot is a special self-defense class for women, taught at noon once a week for 8 weeks at various locations as requested.

Dr. Anderson sees no end to the club for the forseeable future. "The future of the club," he said, "is to continue to provide NIH people a place where they can learn—in a safe, friendly and non-competitive atmosphere—self-defense."—**Susan Pierce** □

Sylvia Funk Awarded First Prize In American University Honors Contest

Fogarty International Center's Sylvia M. Funk has been awarded the first prize in the American University Honors Contest for her undergraduate thesis on Ellis Island. Mrs. Funk attended American University as a STRIDE intern, and graduated this year magna cum laude with honors in history.

The Honors Committee of AU noted that Mrs. Funk's essay, which took sharp issue with the popular view of Ellis Island as an "Isle of Tears," had made an original and creative contribution in her field.

Particularly interesting are the conditions under which U.S. Public Health Service physicians worked during the first two decades of this century, the peak years of immigration.

"The medical officers had the grinding job of trying to identify the physical and mental disabilities of a different individual every 6 seconds throughout a 12-hour day, 7 days a week.... Indeed, line medical inspection at Ellis Island became regarded by the profession as one of the 'best schools for physical diagnosis in the world.'"

Early this spring, another paper by Mrs. Funk, on Brazilian-U.S. relations, won the first place award at the Regional Conference of Phi Alpha Theta, the International Honor Society in History. During her last year at American University, Mrs. Funk served as the undergraduate representative on the History Council.

Mrs. Funk holding the essay which won her first place in the AU contest.

A former employee of NCI, Mrs. Funk was selected for the STRIDE Program by Dr. Philip Schambra, Chief, International Coordination and Liaison Branch, FIC, who served as her supervisor/advisor for the 2½ years of her internship. □

Mary Dasher Retires After 20 Years at NIH

Mary Dasher, a fellowship technical assistant in the International Research and Awards Branch, Fogarty International Center, retired recently after 21 years of Government service.

Mrs. Dasher's entire career has been devoted to the international activities of DHHS except for a year in Florida with the Social Security Administration. Her first 3 years at NIH were with the Visiting Program and later with the International Research Fellowship Program. In 1975 she transferred to the newly established Senior International Fellowship Program and in 1982 became involved with the fellowship programs for U.S. scientists supported by foreign organizations.

During her years of Government service, Mrs. Dasher has been the recipient of several honors and awards. In 1980 and 1981, she received a Group Award. In 1974, she was awarded a certificate of recognition and appreciation of special achievement.

Her coworkers and friends honored her at a reception, and FIC Director, Dr. Craig K. Wallace, presented her with the John E. Fogarty International Center Service Award. Mrs. Dasher is the first recipient of this award; her loyalty and dedication to the goals of FIC were instrumental in the initiation of this award.

Mrs. Dasher (c) received the John E. Fogarty International Center Service Award at her retirement party from Dr. Craig K. Wallace (l) while Dr. Bettie J. Graham, chief, International Research and Awards Branch, looks on.

MEDLINE Subsets Offered To Individuals, Institutions

The development of sophisticated and relatively low cost mini- and microcomputers has prompted the National Library of Medicine (NLM) to offer subsets of its well known MEDLINE bibliographic data base for use on personal and institutional computers. A subset licensing policy and agreement have been adopted, and the Library is now prepared to provide citations from MEDLINE and its backfiles on magnetic tape (and later on diskettes) for storage and reuse locally.

MEDLINE (MEDLARS Online) and its backfiles contain citations to articles from some 3,000 journals. MEDLINE is part of the Library's computerized system, MEDLARS (Medical Literature Analysis and Retrieval System).

Those wishing to receive MEDLINE subsets are allowed considerable latitude in defining the portion of the data base they require. More than 4 million citations from biomedical journal articles from 1966 to the present are available. Subsets may be defined by subject, time period, language of publication, journal title, and other delimiting factors.

Information Varies

The amount of information in each record may vary with the needs of the requester—citation only, citation with indexing terms, citation with abstract, etc. Requesters may lease a one-time subset or elect to receive monthly or quarterly updates as new citations are added to MEDLINE.

The charge for the service varies with the size of the subset and the medium of distribution, whether updates are chosen, and whether the subset is intended for use by one person or by more than one in an institutional setting. In setting prices, the Library recovers the costs of providing the subsets, including NLM computer costs, materials, shipping, staff costs, and overhead.

Those leasing subsets are prohibited from republishing, duplicating, or offering the subset for sale to others.

For an information packet on how to order subsets write to: MEDLARS Management Section, National Library of Medicine, Bldg. 38A, Rm. 4N421, Bethesda, MD 20209. □

Former Fogarty Scholar Gets Israel's Top Science Prize

Dr. Meir Wilchek, a former Fogarty International Center Scholar-in-Residence, was awarded Israel's most prestigious prize in science, the Rothschild Prize for 1984, at a ceremony of the Israeli Parliament on June 10.

The prize was given for work he initiated at the National Institutes of Health, together with Drs. Chris Anfinsen and Pedro Cuatrocasas, on affinity chromatography.

Dr. Wilchek was a Fogarty Scholar during 1981 and 1983 and was also a postdoctoral fellow at NIH from 1966 to 1968. He is presently chairman of the Biophysics Department at the Weizmann Institute of Science in Rehovot, Israel. □

Dr. Philip Schambra Joins U.S. Embassy in India

The Fogarty International Center is bidding a temporary farewell to Dr. Philip E. Schambra who has assumed the post of Science Attache at the U.S. Embassy in New Delhi, India. He will be replacing Dr. Dennis Johnsen of NIH, who has held this position for the past 4 years.

Dr. Schambra

Dr. Schambra will work with the Embassy's Science Counselor, Mr. Ahmed Meer, and U.S. Ambassador to India, Mr. Harry Barnes, to oversee and coordinate DHHS cooperative activities with the Indian biomedical and health services research community.

Based in New Delhi

From his base in New Delhi, Dr. Schambra will also be responsible for oversight and coordination of cooperative activities between DHHS agencies and counterparts in Pakistan, Burma, Sri Lanka, Bangladesh, and Nepal.

For the past 3½ years, Dr. Schambra served as chief of the International Coordination and Liaison Branch, FIC, which is responsible for overseeing and facilitating the participation of NIH Institutes in bilateral cooperative research agreements with foreign countries. Dr. J. R. Schmidt will take over his responsibilities as Chief, ICLB, FIC.

Dr. Schambra received his undergraduate degree from Rice University, and a doctoral degree from Yale University. He worked under a research fellowship from the Institut feur Strahlenbiologie, Karlsruhe, Germany, from 1962 to 1963. He also did research under a fellowship from NASA at the University of California at Berkeley.

Received NIH Merit Award

Before leaving for India, Dr. Schambra received an NIH Merit Award "for exceptional creativity and achievement in carrying out the Fogarty International Center's responsibilities for the coordination of international relationships of the National Institutes of Health." He will return to FIC after ending his tour of service in India. □

A practical man is a man who practices the errors of his forefathers.—Benjamin Disraeli

Fish-Borne Bacterium Can Cause Rampant Blood Poisoning

Vibrio vulnificus—a bacterium which can cause blood poisoning, shock, and severe hypotension (low blood pressure) in persons with liver disease—has been isolated from 80 sites along the Atlantic coast from Miami to Portland, Me.

Although only about 100 cases of Vibrio vulnificus infection have been reported to the Centers for Disease Control in Atlanta, the consequences of this infection can be severe for persons with chronic cirrhosis, hepatitis, and other liver diseases that cause higher-than-normal iron levels in the blood.

In research supported by the National Institute of Allergy and Infectious Diseases, Dr. James D. Oliver and colleagues at the University of North Carolina at Charlotte report that a form of blood poisoning known as fulminating septicemia, which causes a greater than 40 percent mortality, apparently is caused by Vibrio vulnificus.

The bacteria enter the body through the digestive tract after a person at high risk eats raw seafood, especially oysters. Few, if any cases, have been traced to eating raw seafood by healthy individuals.

Both healthy and high-risk individuals can occasionally develop a severe Vibrio vulnificus infection in wounds such as those incurred while cleaning or stepping on shellfish, or while harvesting oysters and crabs.

Wound infections are usually minor, but a few cases have been characterized by marked swelling and tissue death requiring treatment with antibiotics, surgery and, on occasion, limb amputation.

It is not practical to prevent exposure of wounds to vibrios, since small cuts and wounds are so common during contact with marine life and coastal waters.

However, food-borne vibrio infections can, according to Dr. Paul A. Blake of the Centers for Disease Control, be prevented by cooking seafoods thoroughly, protecting them from cross-contamination after cooking, and eating them promptly or storing them at temperatures too hot (140°F or higher) or too cold (40°F or lower) to prevent vibrios from multiplying.

Traditional methods of cooking seafood, such as steaming clams only until they open, may be insufficient to sterilize them, Dr. Blake adds.

Vibrio vulnificus is one of at least nine disease-causing Vibrio species in the U.S., but it is the deadliest. The best known, Vibrio cholerae, causes severe diarrhea and frequently—but not always—is sewage-associated.

Vibrio vulnificus is not sewage-associated and abounds, as Dr. Oliver's studies have shown, in coastal waters. He has found the bacterium in seawater, sediment, plankton, and marine animals such as oysters and clams.

Vibrio vulnificus infections that are reported in the U.S. almost always occur during the warm months of May to October.

—**Maureen Mylander** □

Visiting Women Engineers Tour NIH Facilities

The Society of Women Engineers at its international conference recently offered attendees the chance to tour and discuss the diverse and complex NIH facilities.

The tour, coordinated and conducted by Doug Abramson, a mechanical engineer in Division of Engineering Services, included the Clinical Center Clinical Pathology Laboratory, Surgical Intensive Care Units, Surgery Branch Laboratory, the maintenance center, ACRF mechanical systems and the materiel handling distribution center.

Various design, construction, and maintenance techniques applied by NIH engineers were presented to the visitors. Guests left with a feeling for the engineering challenges and demands offered and required by a sophisticated biomedical research and patient care center such as NIH.

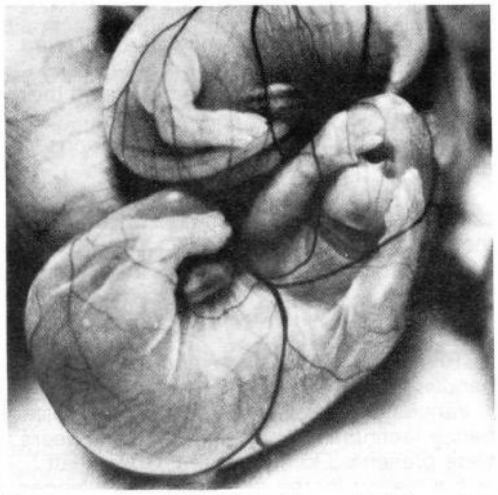
Henry Fulkoski, a dispatcher in the CC Maintenance Section, explains the operation to the visiting women scientists and engineers as Ken Waddell, chief, CCMS (second from l) and Mr. Abramson look on.

Can Babies 'Learn' Before They Are Born? Rat Fetuses Can, NICHD Study Indicates

By Tineke Boddé

Can babies learn before they are born? Can prenatal experiences of unborn infants influence their behavioral development as children and adults? No one knows for sure, but a group of scientists in Oregon has demonstrated that rat fetuses who learned to associate apple juice with physical discomfort, continued to show a dislike for apple juice after birth.

The study, supported by the Human Learning and Behavior Branch of NICHD, was carried out by Dr. William P. Smotherman of Oregon State University in Corvallis, and Gregory Stickrod, M.S., and Dr. Daniel P. Kimble of the University of Oregon in Eugene, Oregon. The research involved 48 rat fetuses, and was based on the knowledge that fetal rats swallow amniotic fluid in the latter part of the 22-day pregnancy.



Rat pups show little liking for apple juice after prenatal aversive conditioning, according to studies by a group of Oregon psychologists. Shown here is a 20-day old rat fetus opening its mouth. *Photo by Dr. William P. Smotherman, Oregon State University.*

On the 20th day of gestation, the researchers gave four groups of 12 rat fetuses a combination of injections. The first group received apple juice into the amniotic fluid followed by a lithium chloride injection into the abdominal cavity to induce gastrointestinal illness.

The second dozen received a saline injection into the amniotic fluid followed by lithium chloride in the abdomen. The third received apple juice into the amniotic fluid and saline in the abdomen, and the fourth was given one saline injection into the amniotic fluid and one saline injection into the abdomen. The last three groups served as controls.

Two days later the rat pups were delivered by cesarean section and placed with foster mothers whose own litters had been removed. Sixteen days after the pups' birth, the investigators painted the nipples of the nursing foster mothers with either apple juice or saline.

When the pups were allowed to approach and suckle the nipples, the group that had received the apple juice linked with the lithium chloride *in utero* showed the least preference for the apple juice coated nipples (43 percent of the time).

The pups from the three control groups preferred the apple juice coated nipples 60 percent, 59 percent, and 64 percent of the time, respectively. The scientists concluded that 20-day-old rat fetuses are sufficiently developed to learn and retain a conditioned taste aversion which may guide later behavior.

To determine whether just smelling apple juice after birth would affect the pups' behavior, Dr. Smotherman conducted a similar experiment as before but he released the *odor* of apple juice near the mother rat instead of painting her nipples with the juice. He found that it took the conditioned rat pups about twice as long as the controls to run the 20-cm.-long runway toward their mother and some did not reach her at all within the 100 seconds allotted.

"These findings indicate that brief exposure of rats to chemical stimuli before birth can have long lasting effects on their behavior and physiological responsiveness as adults," Dr. Smotherman said.

Present and future research seeks to further explore the earliest age at which *in utero* conditioning is possible, whether male fetuses respond differently than females, and how chemosensory stimulation of the rat fetuses affects fetal activity.

"This work is one of a series of branch-supported studies on prenatal behavioral development," said Dr. Norman A. Krasnegor, chief of the Human Learning and Behavior Branch. "It is an excellent example of the rigorous research now being conducted in this new frontier of behavioral science." □

Dr. A. Lilienteld, Pioneer In Epidemiology, Dies at 63

Dr. Abraham Lilienfeld, recognized internationally as a pioneer in the development of chronic disease epidemiology, died Aug. 6 in Baltimore at age 63. A University Distinguished Service Professor at the Johns Hopkins School of Hygiene and Public Health and an alumnus of the School, Dr. Lilienfeld was active as a teacher and scientist until his death.

He was associated with NIH as a consultant and advisor at various times over the last three decades.

"His contributions to the epidemiology of chronic disease have been extensive and of seminal importance," says Dr. D. A. Henderson, dean of the School of Public Health. "So important were they, that Dr. Lilienfeld is often referred to as the father of contemporary chronic disease epidemiology."

Among his many prestigious awards was a Research Career Award from NIH.

He is survived by his wife, the former Lorraine Zemil, three children, Julie, Saul, and David, and five grandchildren.

MIDER LECTURE

(Continued from Page 1)

The Mider Lecture series, begun in 1968 as part of the NIH Lecture Series, to honor the distinguished service of Dr. G. B. Mider, a former NIH Director of Laboratories and Clinics. The lecture is awarded each year to an NIH scientist in recognition of outstanding scientific achievement and serves as an exchange of research information.

Noted for Work on Enhancers

Dr. Khoury is noted for his work in elucidating and describing "enhancer sequences," genetic elements that activate and regulate certain genes. Understanding how enhancers work may help to explain why a body's cells, virtually all with the same genes, can be as different as blood cells and brain cells.

Enhancers may also control the genes that allow some cells to do specialized work, such as making antibodies. In some cases, the presence of enhancers may contribute to the transformation of normal cells into cancer cells.

Dr. Khoury received his undergraduate degree cum laude from Princeton University in 1965. He received his medical degree in 1970, also cum laude, from Harvard Medical School, where he studied virology with Nobelist Dr. John Enders. Dr. Khoury completed his internship at Massachusetts General Hospital in internal medicine before coming to NIAID in 1971.

At NIAID, he started research with Dr. Malcolm Martin on gene transcription and gene expression, using as model systems the small DNA tumor viruses.

In 1976, Dr. Khoury was named head of the virus tumor biology section in NCI's Laboratory of Molecular Biology, and became chief of the laboratory in 1980.

Dr. Khoury received the 1977 Outstanding Young Maryland Scientist Award and the 1981 Arthur S. Flemming Award. He belongs to many professional societies and serves on the editorial boards of the *Journal of Virology* and of *Cell*. □

BIOMEDICAL PROJECT

(Continued from Page 1)

search," said Dr. Frederickson.

"This unique public-private partnership," said Dr. Wyngaarden, "will be an important addition to America's capacity for maintaining its leadership in medical research and health care."

NIH, the Federal government's major biomedical research component, supports biomedical research and training at medical schools, universities and other institutions around the country. It also maintains an intramural research program with more than 2,000 scientists centered primarily at its Bethesda campus.

HHMI, founded in 1953, is one of the largest private medical research organizations in the world. HHMI includes among its programs the maintenance of biomedical research laboratories affiliated with more than 12 research-intensive teaching hospitals and academic medical centers over the United States. □

New National Study on Premature Births Announced by HHS Secretary Heckler

Inauguration of a major national study on the cause and prevention of premature births has been announced by HHS Secretary Margaret M. Heckler. The findings from this study could represent a major turning point in efforts to reduce the number of babies born prematurely, she said.

The study of 15,000 pregnant women over the next 4 years will examine the role of bacteria in stimulating early labor. The National Institute of Child Health and Human Development will oversee the $6.8 million project being conducted at five university medical centers around the country.

"More than half of the infant deaths in our country occur in children born prematurely," Secretary Heckler said in announcing the study. "Even though infant mortality has been declining, the rate of premature births has not decreased in the past 30 years. By better understanding the causes of prematurity, we hope to accelerate the progress we're making in further lowering infant mortality."

Certain bacterial infections in the female genital and urinary tracts are found more often in women delivering premature babies. The study will determine if these infections cause premature labor and if treatment with antibiotics can prevent early labor from starting.

"Accumulating research suggests that the bacteria causing these infections may be responsible for starting premature labor," according to Dr. Mortimer B. Lipsett, Director of NICHD.

Recent studies on why labor starts indicate that an enzyme, phospholipase Ag, released in the anmiotic membrane surrounding the fetus, may stimulate contractions. Researchers have also found that this same enzyme is released by bacteria that cause genitourinary infections.

In the first phase of the project, women in their sixth month of pregnancy will be tested to determine if the organisms are present. A sample of women who exhibit growth of any of the three organisms being tested but show no other symptoms, will be asked to participate in the study.

Half of the women will be treated with an antibiotic and the other half with a placebo until the 38th week of pregnancy or delivery, whichever occurs first.

After delivery, the outcome of pregnancy and the incidence of babies born prematurely to all of the women will be assessed.

"This important clinical trial has the potential of producing the first effective method of preventing many premature births—a development that would eliminate a tremendous amount of infant death and disability," said Dr. Sumner Yaffe, director of the NICHD Center for Research for Mothers and Children.

The principal investigators are:

Dr. David A. Eschenbach, University of Washington in Seattle; Dr. Ronald S. Gibbs, University of Texas, Health Sciences Center in San Antonio; Dr. L. Stanley James, Columbia University in New York; Dr. David H. Martin, Louisiana State University Medical Center in New Orleans; Dr. Philip J. Rettig, University of Oklahoma Sciences Center in Oklahoma City.

Experts from the National Institute of Allergy and Infectious Diseases will collaborate extensively on the project. □

The Fogarty International Center held its annual awards ceremony June 29 at the Stone House. Dr. Craig K. Wallace, FIC Director, presented the NIH Merit Award to Dr. Morris Jones, chief, Special Foreign Currency Program, for "sustained leadership in developing, guiding, and coordinating NIH's role in the highly complex Special Foreign Currency (PL 480) Program over a 19-year period." Receiving awards for their outstanding contributions to the FIC are (front row, l to r): Frances S. Anderson, International Coordination and Liaison Branch (ICLB); Stephanie J. Bursenos, ICLB; Nanci Brice, Office of the Director (OD); Regina Toler, Office of Administrative Management; (second row, l to r): Wanda J. Pifer, chief, Foreign Scientists Assistance Branch; Dr. Jones; Dr. Wallace; Nancy Dennison, Scholars-in-Residence Branch (SIRB). Not pictured: Josephine Schiaffino, SIRB; Judy Ireland, ICLB; Sondra Laskin, ICLB; and Myra Halem, OD.

Dr. Peter Kerekes, 43, Dies From Heart Attack

Dr. Peter Kerekes, Visiting Scientist in the Section of Medicinal Chemistry, NIADDK, died unexpectedly from a heart attack on July 31, three days short of his 44th birthday.

Dr. Peter Kerekes

Dr. Kerekes was well known for his work on isoquinolin and morphine derivatives. He had spent the last eleven months collaborating with section chief, Dr. Arnold Brossi. His work at NIADDK on unnatural morphinans is presently in press, and his investigation of colchinoids will be presented at the American Chemical Society meeting in Philadelphia, Pa. by one of his colleagues.

He came to NIH from the department of organic chemistry at the University of Debrecen, Hungary. He had just decided to extend his stay for another year.

Dr. Kerekes received a Ph.D. degree from the Kossuth Lajos University in Debrecen, Hungary, studying under Professor R. Bognar. His postdoctoral work was performed with Professor S. Pfeifer at Humboldt University in Berlin, East Germany, and also with Professor G. Snatzke at the Ruhr University in Bochum, West Germany.

He spoke fluent German and English in addition to his native Hungarian,and could read and write Russian. Colleagues in the section were shocked to learn of his death. Dr. Brossi described his colleague and friend as a soft-spoken, talented chemist whose kindness will be sorely missed.

Dr. Kerekes is survived by a brother, Antal.

On Aug. 31, Dr. Brossi will give a memorial lecture at the Central Institute of Chemistry in Budapest, Hungary, on work done by Peter Kerekes entitled "New Results on Colchicine and Congeners."

Attention: Photographers

Join others who enjoy photography as a hobby and share the fun while improving your skills. The NIH R&W Camera Club meets the second Tuesday of the month at 7:30 p.m. The first meeting of the new season will be on Sept. 11, at 7:30 p.m., Bldg. 31, Conf. Rm. 4.

For more information, call Leroy Kerney, 496-3401, or Catherine Quigley, 496-3261. □

NINCDS Clones Gene for Gaucher's Disease, The Most Common Jewish Genetic Disorder

NINCDS scientists have cloned the gene for the enzyme whose deficiency causes Gaucher's disease, the most common Jewish genetic disorder.

Cloning of the gene for glucocerebrosidase, an enzyme that helps regulate fat within a cell, is considered a major step toward improved diagnosis and understanding of this neurological disorder.

"We now have the key to open the door to a large number of experiments with the gene," said Dr. John Barranger of the NINCDS Developmental and Metabolic Neurology Branch.

Dr. Barranger and NINCDS scientist Dr. Edward Ginns predict that continued research will enable them to better describe the different mutations of the gene. These mutations result in three types of Gaucher's disease, two of which affect the nervous system.

If descriptions of the genetic mutations that cause Gaucher's can be improved, more sensitive methods of both prenatal and postnatal diagnosis can be developed, according to Dr. Barranger.

Gaucher's disease affects about 20,000 Americans—many of whom are children. In these patients glucocerebroside, a lipid or fat which is a normal part of every cell, accumulates excessively in body tissues. The abnormal buildup results from an inherited defect in glucocerebrosidase, an enzyme or protein that normally breaks the lipid down.

In young children, the buildup of glucocerebroside can be life threatening. Patients may suffer from spleen and liver enlargement, anemia, and bone problems. Symptoms of the neurologic types of the disease include loss of intellectual function and seizures.

The gene for glucocerebrosidase was cloned by Drs. John Barranger, Edward Ginns, Prabhakara Choudary, Brian Martin, and Gary Murray, all of NINCDS, who isolated pure glucocerebrosidase from samples of human placenta and made antibody to this purified material.

Dr. Barranger and his colleagues used the antibody as a tool to detect clones that produce or express glucocerebrosidase. These clones were isolated from a human cDNA library provided by Drs. John O'Brien and Jeff DeWet of the University of California, San Diego.

To confirm that these were indeed clones of the gene for glucocerebrosidase, the NINCDS research team began describing the amino acid sequence of the enzyme.

Amino acids, the building blocks of proteins like glucocerebrosidase, are arranged in long chains in a unique, identifying sequence. The sequence of these amino acids is determined by sets of nucleotide bases—the hereditary units or components of DNA.

The NINCDS scientists identified 250 of the 400 amino acids that make up glucocerebrosidase, and deduced the sequences of nucleotide bases that determine their arrangement. These nucleotide base sequences were identical to the nucleotide sequences of the clone detected by the antibody—confirmation that the team had cloned the gene for glucocerebrosidase.

The research team plans to use recombinant DNA techniques on the newly cloned gene for glucocerebrosidase as a step toward producing the large quantities of this scarce enzyme needed to treat the nonneurologic form of Gaucher's disease.

The cloning research may also one day enable scientists to replace the genetic material that makes the enzyme. "If we can learn enough about the gene's structure and its operation within the cell," said Dr. Ginns, "gene replacement in tissues such as bone marrow may be feasible within the next 10 years." This research will appear in *Biochemical and Biophysical Research Communications*, Sept. 17, 1984, Vol. 123(2), pp. 574-580.—**Diane Striar** □

Conference on Brain Tumors Planned at NIEHS Center

The National Institute of Environmental Health Sciences/National Toxicology Program and Duke University Medical Center will sponsor a conference on "Brain Tumors in Man and Animals," Sept. 5-6 at the NIEHS Conference Center, Research Triangle Park, N.C.

The conference will emphasize the latest technologies and methods for detecting and classifying brain tumors in humans and animals in *in vivo* and *in vitro* differentiation of spontaneously-occurring and experimentally-induced central neuroepithelial tumors.

Human and veterinary neuropathology experts will discuss the use of rodent models to detect environmental inducers of brain neoplasms.

For further information, contact Jacqueline Russell, NIEHS, FTS 629-3208. □

DR. SEAL

(Continued from Page 1)

Rochester, N.Y.

He completed his residency in medicine and cardiology at New York Hospital-Cornell Medical Center in New York City.

During World War II, Dr. Seal received four battle stars while serving as medical officer aboard the *USS Anthony* in the Central and South Pacific.

After the war, he directed naval medical research units in Georgia, Illinois, and Egypt. In Illinois, he investigated the development and spread of infectious diseases in naval recruits and treatment of bacterial diseases with the antibiotics just coming into common usage. He was among the first to use penicillin to treat streptococcal infections for prevention of rheumatic fever.

Following 2 years as head of Navy's Communicable Disease Control Branch in the Bureau of Medicine and Surgery, Dr. Seal became Commanding officer of the Naval Medical Research Unit No. 3 in Cairo, Egypt, in 1958. There he directed an intensive research program in viral diseases, nutrition, and medical entomology.

In 1961, Dr. Seal became commanding officer of the Naval Medical Research Institute in Bethesda, where he directed a staff of 275 physicians, scientists, and technical specialists in research programs relating to naval personnel both in this country and abroad.

Following his retirement from the Navy in 1965, Dr. Seal began a second career in medical research by becoming NIAID Director of Intramural Research. He rapidly gathered and organized a staff of internationally recognized scientists to strengthen and broaden the Institute's research objectives, particularly in developing new vaccines, including those for bacterial pneumonia, influenza, meningitis, and hepatitis.

He became NIAID's scientific director in 1969 and served as Deputy Director of the Institute from 1975 until 1981 when he was asked to establish the NIH disease prevention research program.

During 17 years at NIH, Dr. Seal provided leadership for several government-wide programs. For 8 years he chaired the NIH cholera advisory committee, with responsibilities for the operation of the Southeast Atlantic Treaty Organization (SEATO) Cholera Program and the Cholera Research Laboratory in Dacca, Pakistan (now Bangladesh). He also played a key advisory role in development of high level containment facilities for recombinant DNA research.

Dr. Seal's excellence as a scientist and administrator won him the Founder's Medal of the Association of Military Surgeons twice; the first Stitt Award of the same association for outstanding contributions in the field of antibiotics; and the Medal of Commendation of the Secretary of the Navy. He served as President of the Society of Medical Consultants to the Armed Forces in 1981.

He was also honored with HEW's Superior and Distinguished Service Awards and, in 1980, was among the first to receive designation as a Meritorious Executive in the Federal Government's Senior Executive Service. In 1983 Dr. Seal was elected to senior membership in the prestigious Institute of Medicine of the National Academy of Sciences.

On June 4, 1976, the University of Virginia School of Medicine observed "John R. Seal Day," highlighting his numerous contributions to infectious disease research.

In March 1983, the Kamal-Seal Biomedical Research laboratory was dedicated in Cairo, Egypt. Named for Dr. Seal and Dr. Ahmed N. Kamal, epidemiologist and founder of the Egyptian public health service, and the only one of its kind in Africa, the Laboratory will provide state-of-the-art facilities for both Egyptian and American scientists to join in the study of infectious diseases in that part of the world.

Survivors include his wife, Frances; a sister, Jane Anne Miller of San Francisco; and a niece, Nancy Miller.

A memorial "John R. Seal Fund" has been established to aid research in international health. Those who wish may donate to this fund by sending a check made out to the "John R. Seal Fund" to the attention of Dr. Kenneth W. Sell, Scientific Director, NIAID; Bldg. 10, Rm. 11C103; NIH; Bethesda, Md. 20205.

The Making of NIH Research Grants (II)

A previous article described the receipt and processing of research grant applications at the NIH, and first review by an initial review group. This article discusses the rest of the process—the preparation of summary statements, project site visits, and the *second level review* by a national advisory council or board (usually called a council).

Summary Statements

Immediately after the initial review group meeting and decision, the executive secretary prepares a summary statement on each application. Often called "pink sheets,"—research project grant summary statements are printed on pink paper—these documents contain a brief description of the proposed project, the review group's critique of the project's strengths and weaknesses, and—for approval recommendations—a priority score and a recommended budget and time limit for the project.

Summary statements are sent to the appropriate institutes for their review and are also automatically and promptly sent to principal investigators following initial group meetings.

Project Site Visits

Review of some applications requires information that can only be gathered at the proposed research or training site. Such site visits may occur before an initial review group meeting, after a deferral recommendation during such a meeting, or occasionally after a council deferral recommendation.

In each case, the executive secretary visits the site with a team of visitors, including initial review group members, a program staff person from the institute, and any other needed consultants. Their report is discussed at the next review group meeting.

Council Review

The second level of review for research grant applications is by the appropriate institute's national advisory council or board. Councils are made up of both scientific and public representatives noted for their expertise, interest, or activity in matters related to the mission of their institute. The 12 to 15 members of each council are appointed for overlapping 4 year terms with about 25 percent of the positions becoming vacant each year.

Councils meet at least three times a year to advise the institute on its programs and priorities as well as to review research grant applications. Their recommendations on applications are based on scientific merit as well as the proposed project's relevance to the institute's programs and priorities.

For many applications, councils vote a group (en bloc) concurrence with the initial review group recommendations. Other applications are discussed individually. These include applications from foreign institutions; those with identified human subject, animal welfare, or potential biohazard concerns; those which received a split vote from an initial review group; those requesting an unusually large budget; or those for which policy issues have been identified.

While councils generally agree with the initial review groups' recommendations, they may modify those recommendations based on policy or program considerations. They cannot change priority scores. If a council disagrees with the scientific merit review, they can return the applications to the initial review group for re-review. Except for individual fellowship applications and certain applications with direct costs of no more than $35,000 a year, grants cannot be awarded without a council's recommendation for approval.

After the council's review, the NIH peer review process is complete. The institute acts on the council's recommendations in deciding which grants will be awarded, based on both scientific merit and program considerations.

Chances for Success

Competition for research funds has become increasingly tough over the years. Thus, the number of competing research project grant (R01) applications has risen dramatically—from 8,596 in FY 1972 to 16,798 in FY 1983. The approval rate has also increased—from 71 percent in FY 1972 to 86 percent in FY 1983—but the award (funding) rate has declined.

For example, in FY 1971, 50.7 percent of the approved applications were actually funded; in FY 1979, 51.6 percent. But in the last several years there has been a marked reversal of this pattern. In FY 1983, only 37.2 percent of the approved competing research project applications were funded.

Still, the situation is not hopeless. In FY 1983, NIH made 5,388 awards, an increase of 361 awards from the previous fiscal year. Furthermore, new principal investigators have been consistently able to enter the NIH extramural research support system at a healthy rate. From 1978 to 1982, new, first-time principal investigators averaged over 28.5 percent of the total number of principal investigators on competing research project grants.

Summary

The NIH peer or dual review system—which separates scientific merit reviews from policy decisions on research areas to be supported—permits a more objective evaluation than would result from a single level of review. This system provides NIH with the best available advice about scientific as well as societal values and needs.

—Samuel Joseloff □

CORRECTION

In the first article on the making of research grants at NIH, published in Aug. 14 issue of *The Record,* it was incorrectly stated that each reviewer used increments of 0.2 in arriving at a numerical rating on the scientific merit of each grant application, using a scale from 1.0—the most meritorious—to 5.0, the least acceptable.

They use increments of 0.1, **not** 0.2.

There are more old drunkards than old doctors.
—French Proverb

Her Royal Highness Princess Mele Siulilkutapu from Tongatapu, Tonga, recently visited NIH and was briefed on the latest developments in research on cancer, asthma, diabetes, ulcers and heart disease by NIH scientists. Dr. Thomas E. Malone, NIH Deputy Director, met with the Princess in the Shannon Bldg. before they departed for a tour of the Clinical Center. (Tonga is located in the southwest Pacific Ocean).

Nominations Open on Hazen Clinical Research Awards

Nomination material is now available for the 1985 Lita Annenberg Hazen Awards for Excellence in Clinical Research. The purpose of the awards is to encourage increased participation in clinical research by physicians. Prizes amounting to $100,000 are awarded: $50,000 (tax free) to an outstanding physician investigator and $50,000 for the support of a research fellow(s).

The award committee will select a physician-investigator or team who will be awarded $50,000 (tax free). An additional $50,000 will be provided for the support, for up to 3 years, of a research fellow or fellows whom the award winner will select as associates.

Past recipients of the awards include: Dr. Jesse Roth, National Institute of Arthritis, Diabetes and Digestive and Kidney Diseases, 1979.

Requests for nomination forms and nominations, which will be accepted until Feb. 28, 1985, should be sent to: Dr. James F. Glenn, President, The Mount Sinai Medical Center and Chairman, The Lita Annenberg Hazen Awards Program; 1 Gustav L. Levy Place, New York, N.Y. 10029, or call (212) 650-8832. □

Scientific Products Exhibit Will Be Held on August 30

A scientific products exhibit conducted by the Millipore Corporation, Bedford, Mass., will be held on Aug. 30 in Rm 1A15, Bldg. 37 on Thursday, Aug. 30 from 11 a.m. until 1 p.m. The Continental Water Systems and Waters Associates will also participate. Latest and newly improved products will be presented. Professional personnel will be available for consultation.

Scientific personnel are invited to attend. □

Malaria Gene Cloned by New Technique

A new genetic engineering technique developed by Dr. Thomas F. McCutchan and his colleagues at the National Institute of Allergy and Infectious Diseases (NIAID), brings development of an effective malaria vaccine closer to reality. The technique, described in the Aug. 10 issue of *Science,* enables scientists to cut intact genes (DNA segments) directly out of the genome (the basic genetic blueprint) of the malaria parasite.

In a second article in the same issue of *Science,* Dr. John B. Dame and other NIAID scientists working in collaboration with investigators from the National Cancer Institute (NCI) and the Walter Reed Army Institute of Research (WRAIR), applied the technique to *Plasmodium falciparum,* a parasite causing the most virulent form of human malaria.

They succeeded in cloning the gene for the complete major antigen of the sporozoite, the form of the parasite injected by an infected mosquito. This opens the door to large scale synthesis of the antigen, which in turn could be tried as a vaccine, priming the immune system to kill sporozoites at the very beginning of malarial infection.

Earlier studies by NIAID-supported scientists at New York University (NYU) showed that a sporozoite vaccine can protect humans from malaria. The vaccine was made by irradiating infected mosquitoes and then allowing them repeatedly to bite volunteers. The injected sporozoites, made harmless by the X-rays, stimulated the body's immune system to produce protective antibodies. Follow-up injection of virulent sporozoites did not cause disease.

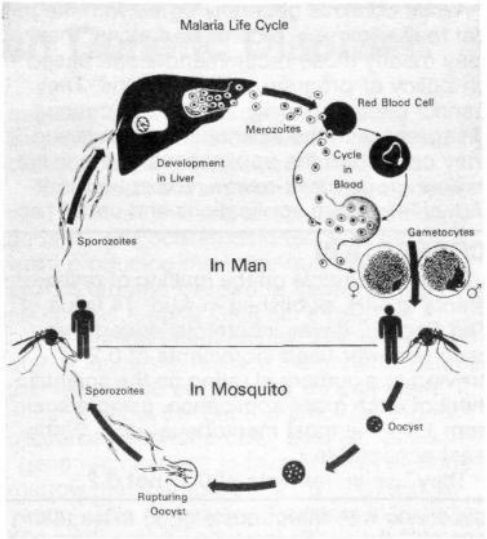
This cumbersome technique was not suitable for a large-scale vaccine program, but it did illustrate the feasibility of protection with a vaccine. Later studies by the NYU group identified the sporozoite antigen that stimulates the immune response of the host. They went on to clone the gene for the sporozoite antigen of the monkey malaria parasite, *P. knowlesi.*

The malaria parasite has three major stages in its life cycle, and unique antigenic components are present at each stage. However, the instructions for manufacture of each antigen are carried in the basic genetic blueprint (genome) of the parasite throughout its life cycle. Until now, instructions have been accessible only during the specific stage during which the antigen is being produced.

The technique developed at the NIAID differs from other cloning procedures in that the scientists are able to cut intact genes directly out of the parasite's genome during any stage of the life cycle and in a form that will produce the complete antigen product. This means that they do not have to work with sporozoites, but they can use the more accessible parasites from the blood (merozoites), which can be maintained in a laboratory culture.

Work with sporozoites is exceedingly difficult. Their natural habitat is the salivary gland of the mosquito, and they cannot be grown or maintained in an artifical medium in the laboratory. Removal of the sporozoites by dissection of the gland is a painstaking process.

After dissection, the sporozoites are cleansed and purified of contaminants, and



copies of the genetic material (messenger RNA) are extracted. Then, more complex procedures are required to reconstruct fragments of genes and isolate DNA clones that produce parts of the major sporozoite antigen.

Malaria remains one of the world's most serious health problems. Increasing numbers of drug-resistant parasites and insecticide-resistant mosquitoes are overwhelming control efforts and contributing to a resurgence of the disease. In the last 10 years, the number of cases doubled worldwide. In some places, it increased 30 to 40 times.

The World Health Organization (WHO) reported 150 million new cases of malaria in 1981, with an estimated 215 million persons chronically afflicted with the disease. In Africa alone, malaria kills more than one million people each year, most of them children under the age of 5.

The importance of a malaria vaccine is increasingly recognized. However, development is complicated by many factors, including antigenic differences of several types of *Plasmodium* parasites that cause disease. The use of this new technique will enable researchers to quickly find and examine important genes from each of the parasites that cause most human malaria.

As an indication of the possibilities, Dr. Dame and his colleagues note in their *Science* article that they have already discovered new regions of the *P. falciparum* sporozoite antigen that may be useful targets for vaccine development.

The new genetic engineering technique was reported by Drs. McCutchan, Joanna L. Hansen, Dr. Dame, and Judith A. Mullins, Laboratory of Parasitic Diseases, NIAID. The cloning of the gene for the sporozoite antigen was reported by Drs. Dame, NIAID; Jackie L. Williams, (WRAIR); Drs. McCutchan, NIAID; James L. Weber, Robert A. Wirtz, and Wayne T. Hockmeyer, WRAIR; Greg S. Sanders, and Dr. E. Premkumar Reddy, NCI; W. Lee Maloy, NIAID; J. David Haynes, Imogene Schneider, Donald Roberts, and Carter L. Diggs, WRAIR; and Dr. Louis H. Miller, NIAID. □

—Patricia Randall

U.S. GOVERNMENT PRINTING OFFICE 1984—421-134/24

DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
National Institutes of Health
Bldg. 31 Room 2B-03
Bethesda, Maryland 20205

Official Business
Penalty for Private Use $300

Postage and Fees Paid
U.S. Department of H.H.S.
HHS 396