

the



Record

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

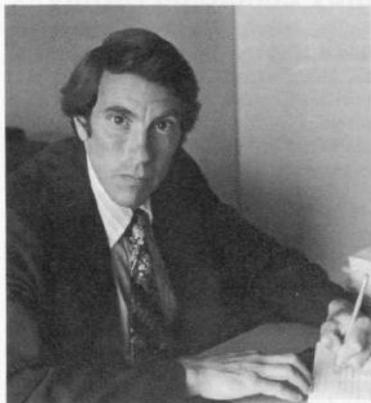
September 7, 1977
Vol. XXIX, No. 18

NATIONAL INSTITUTES OF HEALTH

Wm. M. Doak Is Chief Of Extramural Services Branch in Eye Institute

William M. Doak has been appointed chief of the Extramural Services Branch of the National Eye Institute.

The Extramural Services Branch, formerly the Contracts and Grants Branch, is responsible for the business management of research grants, coordination of research contract activities, and operation of the Institute's management information system under



Mr. Doak has twice received HEW Sustained Superior Performance Awards.

NEI's Extramural and Collaborative Program, headed by Dr. William F. Raub, NEI associate director.

As chief of the Branch, Mr. Doak will play an active role in the planning and coordination of the Institute's cooperative clinical trials of new eye surgery and medical procedures.

A graduate of Pennsylvania State University, Mr. Doak came to NIH in 1966 as a management intern, following which he worked as an administrative assistant in the National Institute of Allergy and Infectious Diseases and as assistant administrative officer in the National Institute of Child Health and Human Development.

In 1971 he was appointed administrative officer for the Division of Extramural Affairs of the National Heart and Lung Institute.

From 1974 to 1976 Mr. Doak was a member of the Staff of the President's Biomedical Research Panel.

Environmental Safety Branch of DRS Is Model for Nation's Scientific Community

Most people know NIH as a pacesetter in medical science. But just as important is NIH's role as a model to the scientific community in the area of environmental health and safety. Rarely does the lab safety issue surface in the public's view—the current controversy over recombinant DNA experiments is an exception. That safety usually remains a behind-the-scenes concern is a testimony to the success of the safety efforts.

NIH Lecture by Dr. Perutz Cancelled Due to Illness

Due to the illness of Dr. Max Perutz, the NIH Lecture to be presented here on Sept. 19 has been cancelled.

Dr. Perutz, Nobel Laureate, Director of the Medical Research Council, and Chairman of the Laboratory of Molecular Biology at Cambridge, Great Britain, had been scheduled to discuss Fundamental Research in Molecular Biology: Its Relevance to Medicine.

It is hoped that his lecture can be rescheduled for a later date.

Safety at NIH has many facets—general plant, biohazards, laboratory, radiation use, and industrial hygiene.

Activities Coordinated

The activities are coordinated by Dr. Rudolf G. Wanner, associate director for Environmental Health and Safety, Division of Research Services.

He is assisted by Vinson R. Oviatt, chief of the Environmental Safety Branch, DRS, and by Michael Musachio, chief of the Radiation Safety Branch.

Their work is coordinated with the Office of Occupational Medicine Service, the Occupational Safety and Health Administration, and other related agencies.

Members of the professional staff (See SAFETY MODEL, Page 9)

Diabetes Day Meeting Tells Practicing Doctors Latest Clinical Advances

Diabetes Day, a 1-day symposium on the skillful management of the diabetic patient, will be presented Saturday, Sept. 24, from 8 a.m. to 5 p.m. in the Masur Auditorium.

Designed for the practicing physician, physicians in training, and allied health professionals in the field of diabetes, the program will focus on the transfer of new advances in the treatment of diabetes mellitus from the clinical research laboratory to practical application.

Features Experts

Lectures and panels will feature recognized authorities on various aspects of diabetes management, interspersed with frequent discussion and audience participation.

The symposium will consider foot care for the diabetic as well as practical problems in the management of diabetes in pregnancy.

Kidney transplants and the challenges posed by diabetic nephropathy, and a review of difficulties in interpretation of the oral glucose tolerance test will also be presented.

Completing the agenda are discussions on adverse reactions encountered in the use of insulin (See DIABETES DAY, Page 8)

Breast Cancer Screening Panel To Examine Issues And Consider Programs

The issue of breast cancer screening will be examined at a meeting Sept. 14, 15, and 16 in the Masur Auditorium in daily sessions from 8:30 a.m. to 6 p.m.

Sponsored by NIH and the National Cancer Institute, the meeting will deal with large-scale breast cancer screening, including the use of X-ray mammography in routine screening programs.

A panel of leading scientists and clinicians, along with lay people, will hear a series of presentations by individuals who have been active in the continuing discussion of breast cancer screening.

Brief presentations will also be made by other concerned professionals and the public.

May Reach Consensus

Following the formal presentations, the panel will attempt to reach a consensus on modalities for breast cancer screening in terms of risk and benefit.

Dr. Samuel O. Thier, department of internal medicine, Yale University, is chairman of the NIH/NCI consensus development meeting.

The panel will consider the question of screening to detect breast cancer in apparently healthy women.

The screening techniques to be considered are medical history, physical examination, mammography, thermography, and breast self-examination. They also will consider alternatives to screening programs and populations and ages appropriate for screening.

Recommendations Expected

The panel is expected to make recommendations for breast cancer screening programs now available through medical care systems.

If indicated, the panel will define clinical trials required to provide additional information pertinent to breast cancer screening.

Among the materials to be presented to the panel are a review of three reports submitted to NCI in March 1977.

These evaluated the potential benefits of mammography based on (See SCREENING, Page 10)



Dr. Wanner, who received his M.D. degree from the University of Tuebingen, Germany, was a medical training officer in epidemiology and surveillance activity at the Center for Disease Control in Atlanta before coming to Bethesda in 1974.

the  **Record**

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NIH Gang Loses to WWDC Wonders in PEF Game

Good times and high spirits won out over thunderstorms and lightning as the WWDC Radio Wonders gassed the NIH Gashouse Gang at the Second Annual Patient Emergency Fund Softball Game at Georgetown Prep on Aug. 8. The final score was 10 to 5.

Over \$800 was raised for the Fund which provides financial assistance for many Clinical Center patients.

A variety of baked goods were donated by R&W members, CC nursing staff, and other NIH staff members.

Door prizes were awarded quickly by master of ceremonies Frank Herzog, TV Channel 9 sportscaster, and Capitals hockey player Hartland Monahan as the rains descended over 200 spectators.

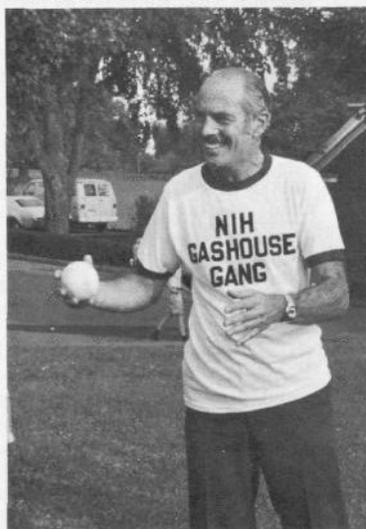
The most coveted prize of the evening, the official softball autographed by President Jimmy Carter, went to young David Lyon.

To contribute to the PEF, send contributions to the CC Social Work Department, Bldg. 10, Room 7D-53.

Registration for Fall Courses To Begin at USDA on Sept. 17

Registration for fall quarter courses at the Graduate School, U.S. Department of Agriculture, will be held Sept. 17-24 in the USDA Patio, North Bldg., located on Independence Ave. between 12th and 14th Streets, S.W., Washington, D.C.

To get a listing of over 600 job-related and leisure courses being offered this fall, call the Graduate School, 447-4419.



Dr. Mortimer Lipsett, CC Director, throws the first ball to start the game.

NIH Singers To Begin Rehearsals on Sept. 18

The NIH Singers, an *a cappella* chorus, will begin rehearsals Sunday, Sept. 18 for their annual holiday concert.

New participants in all sections are welcome. No auditions are held, but an ability to sight-read choral music is required.

Subsequent rehearsals of the R&W-sponsored group will be held every other Sunday evening in the homes of members.

Madrigal Group Meets Sunday

A smaller group, the NIH Madrigal Singers, will meet on alternate Sunday evenings. For further information, contact Dr. Lewis M. Norton, Ext. 61686.

Randy Schools Is New R&W General Manager



Mr. Schools is active in Big Brothers of Washington, D.C., and the Sierra Club.

Randy Schools, general manager of the Recreation and Welfare Association since June, came to NIH after reading a newspaper advertisement for his position.

Already he is drawing on his previous retailing experience—with Garfinkel's and Lansburgh's department stores, and with Webster Clothing, Inc. of Baltimore.

He says he is looking to find new avenues for increasing R&W business, including an appliance-of-the-month purchase special, regularly publishing a more extensive *Smoke Signals*, and planning shorter group trips on a 1-day or weekend basis.

He also plans to upgrade merchandising programs, including more handicrafts. More events may center around family participation, for instance a family picnic now being planned for Oct. 15 at Ft. Meade. Also, he hopes to make additional provision for the interests of patients at NIH.

Mr. Schools received his Masters of Liberal Studies degree in economics and philosophy from Georgetown University this year, and his Bachelor of Science degree from the University of Baltimore in 1967. He is also a graduate of the U.S. Army Intelligence School and served as a counterintelligence agent.

NIH Singles Plan Sept. 8 Cocktail Party in Rockville

Members of the NIH Singles Club are invited to a cocktail party at the Paradise Restaurant (D.C. end of Congressional Plaza, Rockville Pike) on Friday, Sept. 8, from 5:30 to 9 p.m., with a cash bar. Members may bring hors d'oeuvres to share.

Membership applications are available at the R&W desk, Bldg. 31, Room 1A18, Ext. 66061. The next business meeting will be Sept. 22 at noon, Bldg. 31, Conference Room 4, A wing.

Hispanic Heritage Week Celebrated in Programs Planned for Sept. 12, 13

President Carter has issued a formal Proclamation designating the week of Sept. 11 through 17 as National Hispanic Heritage Week 1977.

Americans will be asked to join in celebrating the significance of this week which recognizes Hispanic contributions to the economic, social, and cultural growth of the U.S.

Activities Listed

NIH will sponsor a cultural program on Sept. 12 and 13 in the Masur Auditorium. Everyone is invited to attend.

Monday, Sept. 12, 11:30 a.m.—Introduction, Welcoming Remarks by NIH Director Dr. Donald S. Fredrickson, Ena Camargo's Flamenco Group.

Tuesday, Sept. 13, 11:30 a.m.—Introduction, Rene Noda (singer), Rene Montes' Mariachis.

Tuesday, Sept. 13, 8 p.m.—Introduction, Grupo Folklorico Chile.

D.C. Resident-Employees May Campaign Locally

The Civil Service Commission has added the District of Columbia to the list of municipalities and political subdivisions where employees subject to the Hatch Act may be candidates and otherwise campaign for local office.

The Commission's action permits Federal and D.C. government employees residing in the District to take an active part in campaigns and elections for the offices of mayor, chairman of the Council, and member of the D.C. Council, as independent candidates or in support of or opposition to independent candidates.

Prohibits Non-Local Activities

However, employees subject to the Hatch Act may *not* engage in non-local partisan political activity (e.g., campaign for election of the non-voting Delegate to the House of Representatives) or be candidates or support or oppose candidates of a partisan political party.

Westwoods Win NIH Golf Ass'n 'Stroke' Play Title At Outing

The Westwoods wrapped up the NIH Golf Association *stroke* play title June 27 at the Washington Golf Course.

Their five best net scores totaled 356, a 6-over-par score, and they finished with 23 points to 20 each for the runner-up Ball Hawks and Oafs.

Seventy-six NIHGA members participated in the outing at the Washingtonian with three producing subpar net scores. Earl Kusumoto, of the Brain Waves, who fired a gross score of 76, was the only golfer to break 80.

'Outstanding' Summer Employees Honored



Ms. Stroman and Mr. McKay were honored as outstanding supervisors by summer employees at the recent eighth annual awards ceremony.

One hundred and eight summer employees were cited as outstanding at the Eighth Annual Summer Employee Awards ceremony on Friday, Aug. 19, held in the Masur Auditorium.

Rosalie Stroman, chief of the Readers Services Section, NIH Library, Division of Research Services, and Arthur G. McKay, coordinator of Emergency Preparedness, ODA, were named outstanding supervisors by the summer employees. Keynote speaker Leon M.

Schwartz, Associate Director for Administration, NIH, challenged summer employees to seek excellence in their future careers as scientists, physicians, and administrators, as well as in the broad range of employment fields, to aid an institution such as NIH in its commitment to improving health.

The ceremony officially marked the end of this year's summer employment program which had the largest number of summer employees in its 8-year existence.

Advance Registration Required for One-Week Course in Endocrinology

A 1-week course, A Review of Endocrinology: Diagnosis and Treatment, to be given Sept. 26-30, has been announced by the Foundation for Advanced Education in the Sciences.

NIH'ers Conduct Course

The faculty of the Combined Endocrinology Training Program of NIH will conduct the course in the Clinical Center.

The course will include both didactic and problem-oriented sessions from 9 a.m. to 6 p.m. daily.

Thyroid and adrenal disorders, hypoglycemia and diabetes, calcium metabolism, growth and development, and gonadal function will be covered in detail.

The course content will be suitable for applicants to the subspecialty board examinations in Endocrinology and Metabolism and carries AMA Category I credit.

A fee of \$225 covers tuition and syllabus; however, fellows in training and full-time NIH personnel may register for \$175.

Register in Advance

Registration must be in advance at the FAES office in the CC, Room B1-L-101. A check or a training authorization form must be submitted with the registration form.

Further details may be obtained by calling the FAES Graduate School, Ext. 65272.

Sept. 14 Health's Angels Begin Wed. After Work Fun Runs



You don't have to run like a rabbit—the mascot of the NIH Health's Angels—to participate in the 1-mile fun runs sponsored for 8 consecutive weeks on Wednesday afternoons starting Sept. 14.

Trophies To Be Awarded

But persons completing four of the runs will receive a trophy. The runs will start from the front of Bldg. 1 at 5:30 p.m.

Contact Dr. Rob Pearce, Ext. 66550, Bldg. 36, Room 3C14, for further details.

Persons wishing to compete in the Lynchburg, Va., 10-Mile Race on Sept. 17 should contact Jay Miller, Bldg. 6, Room 120, for information on registration, entry fees, and accommodations.

Health and cheerfulness mutually benefit each other.—Joseph Addison.

DRR Planning New Strategy This Year: CFC Kickoff Days Will Begin October 3

"We are attempting a totally new approach for this year's Combined Federal Campaign effort," explains Ted Nilsen, coordinator for the 1977 campaign and budget analyst in the Division of Research Resources, the lead B/I/D for this year's campaign.

DRR Director Dr. Thomas Bowery is vice chairman, and NIH Director Dr. Donald S. Fredrickson is chairman of the campaign.

"Instead of dragging the campaign on for 2 or more months, we hope to have everything wrapped up in just 3 weeks. Our emphasis will be first day contributions. We hope to have people contribute the first time they're contacted rather than delaying their decision for several weeks," as Mr. Nilsen explains.

A staggered schedule has been organized so that each B/I/D will have its own Campaign Kickoff Day.

The first three B/I/D's—DRR, FIC, and NIGMS—will have their Campaign Kickoff Day on Monday, Oct. 3.

The remaining schedule is:

Oct. 4—NCI, NEI, DCRT;

Oct. 5—OD, CC, NIDR;

Oct. 6—OA, NIAMDD, DRS;

Oct. 7—NHLBI, NINCDS,

NIAID;

Oct. 11—DRG, NLM, NICHD,

NIA

"We hope to achieve as high a percentage as possible of people giving on the particular Campaign Kickoff Day for their B/I/D, when each employee will be personally contacted by a campaign keyperson," says Mr. Nilsen.

Seek First Day Contributions

Instead of leaving material with the employee and then returning at a later date, the keyperson will attempt to have the employee make his CFC contribution, preferably through the convenient payroll deduction plan, during that first contact on Campaign Kickoff Day.

"Instead of playing games with each other for weeks, we hope to greatly simplify as well as shorten the campaign, making it as quick and painless as possible," Mr. Nilsen adds.

Every employee who gives on the Campaign Kickoff Day for their B/I/D will receive a stick-on patch with the words, "I am a first-day giver."

Those who receive the patch will be encouraged to wear it throughout the campaign to let their fellow employees know that they contributed on Campaign Kickoff Day.

Records will be kept and posted throughout NIH on the percentage of employee participation for each B/I/D. Special awards will be presented to B/I/D's which achieve 75 percent participation on their Campaign Kickoff Day.

The campaign coordinator points out that 97 percent of the money collected goes to CFC agencies, a

fact which discredits the myth that a high percentage of the collections goes to CFC overhead.

"Most of the CFC workers are volunteers who receive no pay," says Mr. Nilsen, including himself.

This year a traveling rally will tour the NIH campus on Oct. 5, rather than holding a noontime rally in one place.

"With such a wide spectrum of agencies benefitting from CFC support, every employee can identify



Mr. Nilsen, 1977 CFC coordinator, makes plans for the totally new approach to be used during this year's campaign.

with at least one . . . and probably several," Mr. Nilsen points out. "If someone wants to give to a specific agency, they can do so by designating their contribution.

"If people cooperate and get involved, this year's campaign should be a pleasant and successful one. What each person contributes is, of course, up to one's conscience, but we believe everyone should give something."

Film Cites Importance Of CPR Training for All

A 15-minute color film, entitled "A Life in Your Hands," featuring Burt Lancaster, will be shown by the Occupational Medicine Service on Sept. 13, 14, 15, and 19.

This movie is an introduction to CPR (cardiopulmonary resuscitation) and stresses the importance of CPR training for everyone.

It is being offered at the time and places indicated:

Tuesday, Sept. 13, 11:30 a.m. and 12:15 p.m., Bldg. 1, Wilson Hall.

Wednesday, Sept. 14, 11:30 a.m. and 12:15 p.m., Federal Bldg., Room B-119.

Thursday, Sept. 15, noon and 12:30 p.m., Westwood Bldg., Room 428.

Monday, Sept. 19, 11:30 a.m. and 12:30 p.m., CC Masur Auditorium.

NCI Scientists Report Using Vitamin E Cuts Side Effects of Adriamycin in Mice

Vitamin E lessens the harmful effects of the widely used anticancer drug Adriamycin on heart muscle in a strain of laboratory mice, according to scientists at the National Cancer Institute.

The vitamin protected normal tissue without diminishing the drug's activity against cancer in the animals. Dr. William McGuire reported these findings May 19 at the 68th annual meeting of the American Association for Cancer Research in Denver, Colo. Other NCI scientists participating in the study were Dr. Robert C. Young, Karen Grotzinger, and Dr. Charles E. Myers. One of the most active anticancer drugs known, Adriamycin—a commercially available antibiotic—is active against at least 10 forms of cancer in man.

Side Effect Described

Unfortunately, a side effect of the drug is deterioration of the heart muscle that may lead to congestive heart failure. This side-effect has limited the total dose of Adriamycin that any patient can receive to 550 mg per square meter of body surface.

The quinone group of the Adriamycin molecule has been suspected of being responsible for damage to cardiac tissue.

Quinones are known to interfere with the generation of energy in mitochondria and other cell components by producing unstable molecules called "free radicals".

These free radicals set off in the cells a chain of chemical reactions, one of which may be damage to the cell's membrane, resulting in cell destruction.

Interaction Produces Chemical

A chemical called malondialdehyde is produced by the interaction of free radicals and lipids in the membrane.

Examination of heart tissue from mice treated with toxic doses of Adriamycin revealed high levels of malondialdehyde, according to Dr. McGuire, indicating the possibility that free radicals were being produced. Malondialdehyde could not be detected in heart tissue of normal mice.

Because vitamin E reacts with free radicals, preventing their reaction with other compounds, the

NCI scientists postulated that it might protect the heart against Adriamycin-induced cell destruction.

A group of mice was given a single injection of 15 mg/kg of Adriamycin. Malondialdehyde levels peaked after 4 days; 85 percent of the animals died from drug toxicity by the 30th day.

Another group of mice was pretreated with *alpha*-tocopherol, the principal constituent of vitamin E, 1 day prior to receiving an equal dose of Adriamycin.

No elevation of malondialdehyde was seen in this group of mice, and only 15 percent of the animals died from drug toxicity by the 30th day.

Some Destruction Blocked

Examination of heart and other tissues from these animals confirmed that the vitamin E component blocked some destructive changes, Dr. McGuire says.

Free radical scavengers other than vitamin E did not protect mice from Adriamycin toxicity. Other agents tested included ethoxyquinone butylated hydroxyanisole (BHA), and butylated hydroxytoluene (BHT).

When Adriamycin was given to mice on a weekly schedule of 5 mg/kg for 5 weeks, 100 percent of the mice died by 90 days. In a group of mice pretreated with vitamin E, 1 day prior to drug administration, only 60 percent of the mice died by 90 days.

Anticancer Effect Considered

Adriamycin is thought to achieve its anticancer effect by binding to DNA, the cell's hereditary material, and blocking DNA and RNA synthesis. This reaction may be different from that which causes deterioration of heart tissue, the NCI scientist points out.

Vitamin E pretreatment did not block the anticancer activity of Adriamycin in mice bearing the P388 transplanted leukemia. In fact, use of the vitamin led to increased survival by permitting higher doses of the anticancer drug to be administered.

Before these findings in mice can be applied to cancer patients receiving chemotherapy with Adriamycin, additional studies will have to be done, Dr. McGuire said. Information is needed on the effects of the vitamin on Adriamycin's toxicity to human heart tissue and activity against human cancer cells.

Also, the doses of the vitamin required for protection in the



Dr. Stephen J. Benkovic, of Pennsylvania State University, will receive the 1977 Pfizer Award in Enzyme Chemistry at the American Chemical Society's National Meeting in Chicago later this year. His research focuses on the action of enzymes catalyzing phosphoryl group transfer as well as one-carbon unit transfer requiring a folate derivative as co-factor. Dr. Benkovic is a grantee of NIGMS and a former member of the DRG Medicinal Chemistry B Study Section.

WHO Publishes First Oncology Classification

The first edition of the *International Classification of Diseases for Oncology* (ICD-O) has been published by the World Health Organization.

NIH's are Editors

The publication was edited by four NCI scientists: Dr. Louis B. Thomas, chief, Laboratory of Pathology; Dr. Donald Henson, staff pathologist, Laboratory of Pathology; Constance Percy, statistician, Biometry Branch; and Dr. Peter Graepel, formerly of the NIH Division of Computer Research and Technology and the NCI Office of International Affairs, and now with Ciba-Geigy Pharmaceutical Company.

Is Coded Nomenclature

The ICD-O, a supplement to the ninth revision of the *International Classification of Diseases* (ICD-9), is a coded nomenclature for classifying tumors by their anatomic site and morphologic type (histology).

It is the first time an internationally acceptable system has been available for coding benign and malignant tumors in this way.

A 10-digit code number is used for classifying tumors in the ICD-O. The first four are the numbers assigned body sites of cancers in Chapter II of the ICD-9. The next four digits designating histologic type are followed by a slash (/) and the two digits to in-

mouse would represent an equivalent dose for man higher than ever before used.

Research Grants List Is Available for FY 1976

National Institutes of Health Research Grants, Fiscal Year 1976 Funds and Transition Quarter Funds is now available.

The volume presents 15,344 research career program awards and research grants awarded by NIH from Fiscal Year 1976 funds and from funds available for the transition quarter, July 1 through Sept. 30, 1976.

A summary indicating the extent of financial support given by each supporting component is presented.

In addition, grants and awards are shown by recipient area, principal investigator, and the organization having professional responsibility for the work.

Soon to be released are volumes presenting contracts, training, construction, and medical libraries support.

Listings of NIH grants and development contracts are prepared annually by the Statistics and Analysis Branch, DRG.

Single copies of the research grants volume, DHEW Publication No. (NIH) 77-1042, are available free of charge from the Division of Research Grants.

Multiple copies may be purchased from the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402, (GPO stock no. 017-040-00410-9).

dicating "behavior"—cancerous, benign, in situ—and grading and differentiation.

For example, the code number for "well-differentiated squamous cell carcinoma of the cervix" is T-180.9, M-8070/31.

Many of the new terms for cancers and histologic concepts have been included in ICD-O. A special effort was made to list the terms used in the *International Histological Classification of Tumors* (Blue Books) published by the World Health Organization.

The ICD-O is completely compatible with the many records already coded by the *Manual of Tumor Nomenclature and Coding* (MOTNAC) and the Morphology sections 8 and 9 of the *Systematized Nomenclature of Pathology* (SNOP).

Includes Morphology Section

The Morphology section of the ICD-O has been included as the Neoplasm section of *Systematized Nomenclature of Medicine* (SNOMED) recently published by the College of American Pathologists.

Prior to publication, ICD-O was field tested in more than 20 English-speaking countries by coding more than 35,000 diagnoses of tumors.

The ICD-O is being published in (See *ONCOLOGY*, Page 8)



**TAKE
TIME!
MAKE
TIME!**

GIVE BLOOD

NHLBI Issues Its Fourth Annual Program Report

The National Heart, Blood Vessel, Lung, and Blood Program: Fourth Report of the Director of the National Heart, Lung, and Blood Institute (DHEW Publication No. [NIH] 77-1170) is now available on request from the Public Inquiries and Reports Branch, NHLBI.

The report, recently forwarded by the President to Congress, reviews Institute activities, programs, and accomplishments during 1976 and outlines plans and project allocations for the National Program over the next 5 years.

Act Increases Authority

The National Heart, Blood Vessel, Lung, and Blood Act of 1972 increased the authority of NHLBI and directed the Institute and its advisory bodies to prepare and submit to Congress a plan for an expanded, intensified national effort to reduce illness, disability, and death from cardiovascular, lung, and blood disorders.

It further directed that the plan be updated each year and Congress be kept informed of present and projected activities, program progress, and achievements through reports submitted annually by the Institute Director and by the National Heart, Lung, and Blood Advisory Council.

Program Is Joint Effort

NHLBI is the prime mover and coordinator of the National Program; but it is a joint effort involving participation of numerous other Federal agencies, voluntary health organizations, professional societies, and collaborative efforts with other countries, most notably the U.S.S.R.

The National Program is directed against a group of diseases that, collectively, kill over a million Americans each year, and bring illness or disability to tens of millions of others, and cost the economy over \$60 billion in lost wages and productivity and costs of medical care.

The first two sections of the Fourth Report of the Director provide:

Provisions Outlined

- 1) data on the magnitude of the health problems posed by various cardiovascular, lung, and blood disorders;
- 2) historical background on Institute programs prior to and since the National Heart, Blood Vessel, Lung, and Blood Act of 1972; and
- 3) capsule summaries of recent research and clinical achievements stemming from the National Program.

Subsequent sections cover:



Recently NIH Director Dr. Donald S. Fredrickson (seated c) formally signed the negotiated Agreement between the Washington Area Metal Trades Council and NIH, covering non-supervisory employees in the four units for which the Council has recognition: Fabric Care, Grounds Maintenance and Landscaping, Custodial Laborers and Related Building Services, and Transportation Workers. Negotiators included DAS Director Otis Ducker (seated l), Kermit Miller (not in photo), and Donald Isaac (seated r). Other members of the negotiating committee were (l to r): Connie Row, James Neill, Gordon Gamble, William Morton, Clarence Black, and Lorraine Hopkins. Also (not in photo), William Leach, Lewis Joyner, Nathaniel Cunningham, Daniel Kenney, Thomas Cook, and Walter Chakwin.

NIH Research Team Develops Inexpensive Ultrasonic Real-Time Abdominal Scanner

An NIH research team has developed an inexpensive ultrasonic real-time scanner for obtaining a cross-section view of the upper abdomen.

The researchers—Dr. Thomas H. Shawker, William H. Schuette, and Willard Whitehouse of the Clinical Center and Division of Research Services—designed the mechanical sector scanning system which permits simultaneous, continuous viewing of the abdomen.

Ultrasonic scanners operate on the same principle as the sound-echo system of bats which enables them to dodge obstructions while in flight. Bats send out a high-pitched sound that generates a series of echoes when striking an object.

Signals Send Echoes

Similarly, the ultrasonic scanner's pulsed sound signals send back echoes from the various tissue boundaries in the body.

The scanner receives and converts the echoes to electronic signals which are seen on the TV screen as a black and white cross-sectional image of the body.

Unlike conventional static ultra-

1) allocation of manpower and resources;

2) current status and updated 5-year plans for Institute programs in each major disease category;

3) prevention, education, and control programs;

4) joint programs involving NHLBI and other Federal and non-Federal agencies, together with international collaborative efforts; and

5) training programs for the development of additional highly skilled research and clinical manpower.

sonic B-scanners, real-time scanners give a continuous "fluoroscopic" image.

Although real-time scanners have been used for cardiac and obstetrical diagnosis, the investigators designed this scanner to be of maximum value for abdominal study.

The scanner uses a single element ultrasonic transducer which mechanically rotates through a ± 25 degree angle. A counter balancing rotation of the motor and transducer reduces mechanical vibration to a minimum.

Takes Linear Scan

A unique photoelectric feedback control permits a linear scan to be taken.

The unit is inexpensive and can be integrated as an "add-on" to commercially available static B-scanners. Transducers of different diameters and frequency can be interchanged, and the unit is electronically synchronized to a TV system for video recording.

The investigators have examined over 100 patients with the scanner and developed an examination technique for a rapid evaluation of the abdomen.

The unit is easily positioned on the skin, even-angled underneath the rib cage, and allows continuous

Abstracts, Proceedings Available for Oncogenesis, Herpes Virus Symposium

The Third International Symposium on Oncogenesis and Herpes Viruses, held July 25-29 at Harvard University, featured more than 100 oral and nearly as many poster presentations on herpes viruses.

The symposium was cosponsored by the Virus Cancer Program, Division of Cancer Cause and Prevention, National Cancer Institute, and by the International Agency for Research on Cancer (IARC), a component of the World Health Organization.

Included in each of seven sessions were two to four review papers that preceded information presented by scientists from the U.S., Canada, South America, Europe, Israel, Iran, Japan and Australia.

Cover Molecular Structure

The sessions covered the molecular structure of various herpes viruses, cell-virus interactions, host response to herpes virus infection and herpes virus-associated tumors, the role of co-factors and prospects for control of herpes virus-related diseases.

A limited supply of the abstracts is available for \$5 per copy from Dr. Fred Rapp at the department of microbiology, The Milton S. Hershey Medical Center, Pennsylvania State University, Hershey, Pa. 17033.

Proceedings will be published by the IARC in about a year. Published papers from the last meeting, held in 1974 in Nuremberg, are available from the Q Corporation, 49 Sheridan Ave., Albany, N.Y. 12210 (IARC Scientific Publication No. 13, Part I—\$40, and Part II—\$32, prepaid, plus \$1.10 handling).

viewing as the scanner is moved freely over the patient's body.

The resolution is sufficient to visualize the major arteries, veins, and upper viscera with normal physiological activity.

Although the group focused on normal patients for their initial study, the scanner is proving useful for detecting abdominal disease.

The pancreas, liver, and kidneys can be scanned for tumors, major arteries and veins examined for abnormalities, ascites detected, and the gall bladder checked for the presence of stones.

The research group is continuing studies on other applications of the scanner.

As we advance in life, we acquire a keener sense of the value of time. Nothing else, indeed, seems of any consequence; and we become misers in this respect.—William Hazlitt



Animal Center Will Hold Open House This Saturday

The Center is having an Open House on Saturday, Sept. 10, 10 a.m. to 1 p.m. Tours are planned for residents of the Poolesville area. NIH employees and their families also are welcome.

The Center is located on Elmer School Road. To reach it, drive west on Route 107 (White's Ferry Road) and turn left on Elmer School Road. A map is available from the Veterinary Resources Branch (Ext. 62527).

Animal Center in Poolesville

The NIH Animal Center is located on a back stretch of country road near White's Ferry on the Potomac.

Upon entering the grounds one first sees a small herd of horses, and then, in the pasture beyond, two Holstein steers—2,000 lbs. each.

A bit farther down the drive one hears the yelps of dogs, mostly English and American foxhounds. If they are out on their running areas they can be viewed from the roadway. They're very curious about visitors and very friendly, rearing up on their haunches and pressing their wet noses through the chain link fence—a thousand dogs competing for attention.

The horses, cattle, and dogs are just some of the large animals at the 513-acre Animal Center in Poolesville, Md. There also are the cats—including a 20-lb. fellow with a big meow—monkeys, sheep, goats, burros, swine, turkeys, and chickens, all contributing to a host of barnyard smells and sounds.

The Center, established in 1960 on the grounds of a former farm, is managed by the Animal Center Section of the Veterinary Resources Branch, Division of Research Services.

It is headed by Dr. Francis Judge, a veterinarian.

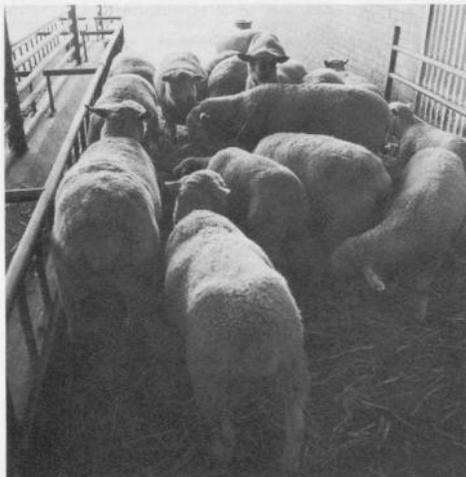
The basic role of the Center is to supply the larger laboratory animals and animal by-products such as blood, serum, and tissue for

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Story and Photos
By Mike Knepler



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Dr. Wolfe (l) and Dr. Judge examine the ears of the largest cat at the Animal Center.

Center in Poolesville Provides Veterinary Resources for NIH

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gators in Bethesda.

The three units and their heads are: primate
quarantine, Dr. David Renquist; ungulates
(hooved stock), Leonard Stuart; and carnivo-
res, Dr. Irving Baas.

Primate quarantine is the primary NIH in-
tramural resource for non-human primates as
it procures, quarantines, conditions, and issues
the animals for research. There are approxi-
mately 1,000 primates, mostly rhesus monkeys.

The ungulate unit is the principal source of
livestock and fowl which provides NIH with
normal blood and immune serum. The unit is
equipped with surgical, radiographic, and pre-
and postoperative care facilities. The unit has
about 1,000 farm animals—10 horses, 11 cattle,

72 burros, 400 sheep, 300 goats, 100 swine, and
50 fowl.

The carnivore unit is the main NIH resource
for research dogs and cats. There are 1,000
dogs, mostly foxhounds, 60 percent of which
are bred at the Center, and 120 cats. The dogs
are used for cardiovascular research and as
blood donors; the cats are used for a variety
of studies, including neurological.

The breeding of the dogs is under the charge
of Dr. Thomas Wolfe, who is very pleased
when someone comments about the friendliness
of the dogs.

Socializing the dogs and the other animals is
a major concern of Dr. Wolfe and the other
Center employees. Most of the employees are
involved in the socializing process, and all like
animals; everyone, Dr. Wolfe says, has a pet
at home. Dr. Judge, in fact, has a pet goat—
goats being his favorite animal.

While the open house primarily is for Pooles-
ville area residents, Dr. Judge hopes more
NIH'ers become aware of the facility. He re-
marked that the Center is underutilized by
NIH researchers and said he would like addi-
tional investigators to spend more time at the
Center, especially using its surgical facilities.

The Center, which includes power and sewage
treatment plants, and security and grounds
maintenance buildings, is cared for by the
Division of Engineering Services and the Division
of Administrative Services. An animal
husbandman, a security guard, and an engi-
neer have residences at the Center.



Dr. David P. Beck Joins NIH Grants Associates

Dr. David P. Beck recently joined the Grants Associates Program for a year of training in health science administration.

The Grants Associates Program prepares biomedical and behavioral scientists for roles as health science administrators.

Dr. Beck graduated from Princeton University in 1966, receiving a B.A. degree in biology. He then went to Johns Hopkins University where he earned the Ph.D. degree in biochemistry in 1971.

For the next 3 years, he was a Helen Hay Whitney Foundation postdoctoral fellow at Harvard University, and in 1974 he joined the Maryland Psychiatric Research Center in Baltimore as a research associate.

Research Noted

Dr. Beck's research interests include membrane biogenesis, membrane structure and function, mitochondrial metabolism, and transport mechanisms.

ONCOLOGY

(Continued from Page 4)

the four official languages of the World Health Organization—English, French, Spanish, and Russian—as well as in Italian, German, Portuguese, and several others.

The editors hope that the ICD-O will promote cooperation in the field of cancer by providing an internationally acceptable coding system for anatomy and morphology.

The ICD-O will be useful in pathology departments, tumor registries, cancer data banks, and many special cancer studies and will be used in all the Comprehensive Cancer Centers that are participating in the Statistical Analysis and Quality Control Program Funded by NCI.

Urge Use at NIH

The editors also suggest that anyone in NIH using a coded nomenclature for tumors consider using ICD-O to accumulate data that are comparable to national and international data banks.

ICD-O is available from World Health Organization booksellers or from the College of American Pathologists, Skokie, Ill.

It is a common error to infer that things which are consecutive in order of time have necessarily the relation of cause and effect.—*Jacob Bigelow*

NIAID-Supported Boston Scientists Study Cellular Immunity in Thyroid Tumors

Boston investigators have reported that medullary thyroid cancer patients—and some of their relatives at risk for the disease—exhibit a specific immune response to thyroid-tumor antigens. These findings support other evidence for an immune response to human, tumor-associated antigens and raise additional questions about the relationship between tumor immunity and cancer.

How the body protects itself against the development of cancer is poorly understood. However, some scientists believe that the cellular immune response—mediated by the lymphocytes—plays a key role.

This response is thought to act as a type of immune surveillance system triggered by the presence of tumor-associated antigens—specific proteins located on the surface of certain cancer cells.

Lymphocytes Increase

In the presence of these antigens, the lymphocytes—functioning as specific immune defense cells—increase in number and produce intermediary substances that fight off cancer cells.

Two laboratory measurements of this response are lymphocyte proliferation and the production of migration inhibitory factor (MIF)—a substance that inhibits the migration of guinea pig macrophages in a capillary tube.

Cellular immunity has been observed in patients with breast and other types of cancer, and, in some cases, in their relatives and in household contacts.

No one knows why certain people develop this response and others do not. Scientists feel that a better understanding of cellular immunity may lead to improved methods of cancer detection and treatment, including immunotherapy.

In the presently reported study, the investigators—partially supported by the National Institute of Allergy and Infectious Diseases—selected a family with a history of medullary thyroid cancer (MTC)—a genetic disease affecting nearly 50 percent of family members.

Disease Is Unpredictable

Although the course of the disease is frequently unpredictable, it is sometimes detectable in the early stages. High levels of calcitonin in the blood—a hormone produced by the thyroid gland—usually indicate a precancerous condition.

Although the role of the cellular response in MTC is unclear, the high frequency of the disease in affected families makes it a good model for studying the clinical significance of the response.

After examining thyroid tissue and measuring calcitonin levels, the researchers divided the 56 family members into four groups according to their clinical status with MTC.

Group I included 18 patients with

the disease; Group II—seven patients with C-cell hyperplasia—an abnormal increase of thyroid cells thought to be precancerous; Group III—12 members without symptoms but genetically at risk for MTC; and Group IV—nine members who had no symptoms and were not considered at risk.

Then, the scientists tested each person's response to normal and to thyroid-tumor antigens. The lymphocyte proliferation response and the production of MIF were used as indicators of a specific cellular immune response.

In addition, 25 normal people were used as controls and five patients with Graves' disease—hyperthyroidism—were included to verify the specificity of the response.

In agreement with previous studies, the researchers found that lymphocytes from 12 of 18 patients with MTC exhibited a specific cellular immune response to thyroid-tumor antigens. In addition, four of the seven patients with C-cell disease exhibited a similar response.

Observe Family Response

Of special interest, according to the researchers, is the fact that 6 of the 12 normal family members at risk for MTC also responded specifically to the tumor antigens. In contrast, cellular immunity was observed in only 2 of the 25 normal subjects and in only 2 of the 9 normal family members not at risk.

Although the presence of a cellular immune response in healthy family members at risk is inexplicable, the researchers suggest that laboratory measurements of cellular immunity may be detecting early C-cell disease in these people. They add, however, that further studies are needed to prove this hypothesis.

More importantly, these findings raise interesting and conflicting thoughts about the role of immunity in the development of cancer. It is not known whether the development of a cellular immune response offers protection against MTC or causes its spread.

Question Role of MTC

If patients with MTC possess cellular immunity to tumor antigen, why did the disease develop and why can't they rid themselves of it?

One explanation, proposed by the investigators, is that the presence of inhibiting blocking factors produced by the tumors prevents cellular immune response from being

DIABETES DAY

(Continued from Page 1)



Dr. Salans will chair discussions at the 1-day symposium on the skillful management of the diabetic patient.

therapeutically, including lipotrophy, allergy, and insulin resistance; and a rational approach to the treatment of diabetic ketoacidosis, a serious consequence of uncontrolled diabetes.

Dr. Lester B. Salans, associate director of the Diabetes, Endocrine and Metabolic Diseases Program, NIAMDD, will chair the discussions.

Register in Advance

Diabetes Day is presented free of charge by the National Institute of Arthritis, Metabolism, and Digestive Diseases. To insure admission, advance registration by mail is recommended.

Send list of registrants to Dr. Jesse Roth, Diabetes Branch, NIH, Clinical Center, Room 8A-243, Bethesda, Md. 20014.

This program is approved for category I credit for continuing medical education.

protective in these people.

To further clarify the role of the cellular immunity in family members at risk, the researchers suggest a clinical follow-up of these people to determine if any of them develop C-cell disease or MTC. In addition, they also recommend following patients with MTC and those with C-cell disease to see whether those with a cellular immune response differ in their long-term survival from those without the response.

The report of this research by Drs. Ross E. Rocklin, Robert Gagel, Zoila Feldman, and Armen Tashjian from the departments of medicine and pharmacology, Harvard Medical School, the departments of medicine, Robert B. Brigham Hospital and Tufts New England Medical Center, and the Laboratory of Pharmacology, Harvard School of Dental Medicine, appeared in the April 14, 1977 issue of the *New England Journal of Medicine*.

All knowledge comes from noticing resemblances and recurrences in the events that happen around us.—*Wilfred Trotter*

SAFETY MODEL

(Continued from Page 1)

possess basic laboratory knowledge, often have backgrounds in biology or chemistry, and are trained in environmental safety and health. Experts in specific areas also aid the program.

On occasion, outside consultants are brought in, primarily to make an independent confirmation of safety test results. NIH safety specialists likewise often are requested to double check the standards of other Federal safety programs.

Dr. Wanner and Mr. Oviatt compare their work and the work of laboratory scientists.

"We Try Harder"

"Like the laboratory scientist, we're never satisfied with the results of our efforts," Dr. Wanner says. "We always try to find something new or better."

The difference, Mr. Oviatt explains, is that their staff is not involved in basic research but only in applied research. "We're here to help the research scientist build safety into the lab," he says.



Mr. Oviatt, a registered professional engineer, has a master's degree in public health and has been chief of the Division of Research Services, Environmental Safety Branch since 1969. A diplomate of the American Academy of Environmental Engineers, he has served from 1975 to date as chairman of the WHO Working Group on Laboratory Safety Elements and on the Council of the International Federation of Hospital Engineering.

Dr. Wanner notes the success of their endeavors but cautions that there seems to be an irreducible margin. "The one thing you always have to keep in mind is that you can't exclude occasional human error, such as accidents, errors in judgment, and other mistakes."

Dr. Wanner has held his current post since December 1974 when NIH combined all its environmental health and safety units into one program. The coordinated effort has served as a model for the

4-Year Framingham Eye Study Reports On Eye Disease, Blindness Epidemiology

An epidemiologic study of factors that may be associated with increased risk of eye disease and blindness has uncovered new clues for research to prevent cataract and macular degeneration—leading causes of blindness in the U.S.

In the Framingham Eye Study, a 4-year cooperative investigation by the National Eye Institute and the Boston University School of Medicine, eye examination data were correlated with information on 550 health-related factors obtained from 2,675 residents of Framingham, Mass.—67 percent of the 3,977 surviving participants in an NIH study of heart disease risk factors since 1948.

The study's principal investigators are Harold A. Kahn, former chief of NEI's Office of Biometry and Epidemiology and now professor of epidemiology at Johns Hopkins University School of Hygiene and Public Health, and Dr. Howard M. Leibowitz, chairman of the department of ophthalmology, Boston University School of Medicine.

The Framingham Eye Study is the first large-scale attempt to determine the prevalence of eye disease in a well-defined and closely-followed population and to identify risk factors associated with eye disease.

Safety Office Relocates

The Safety Office, DRS, has moved to Bldg. 13, Room 2E41. The telephone number remains the same, Ext. 65323.

rest of the scientific community.

Dr. Wanner and Mr. Oviatt are particularly proud that no secondary cases of infection have ever occurred, although lab accidents have happened.

One reason is that waste water from NIH is monitored to make sure no harmful contaminants escape into the community water supply.

They also attribute their success to a safety consciousness promoted at NIH by DRS Director Dr. Joe R. Held and by other key personnel.

"We always have an open line to Bldg. 1," Dr. Wanner says. "NIH Director Dr. Donald Fredrickson himself is very safety and health conscious, and consequently gives us the support we need."

Dr. Wanner stresses the need for program improvements. "It's evolutionary. There are always areas to improve, always needs for training and retraining," he says.

"People always tell me it's an impossible job. But I don't think so, although it's very challenging," he continued. "Our job is to make NIH employees safe and happy."

He smiles. "But while they are not always happy, usually they are safe."

For many years State agencies for the blind were the principal source of data on the prevalence and incidence of visual disorders and disabilities.

The value of this information is limited however, because it is restricted to cases of legal blindness and because the number of blind persons not registered with the State agencies is unknown.

Fred Ederer, chief of the NEI's Office of Biometry and Epidemiology, notes that on the basis of State data one would have expected to find about 7 legally blind people in a population with sex and age characteristics of the Framingham Eye Study group.

Blindness Underregistered

Instead, the Framingham investigators found that 22 of the 2,675 people screened were legally blind. This suggests a substantial under-registration of blindness with State agencies.

Members of the Framingham population were screened during 1973-75 for senile cataract, senile macular degeneration, open angle glaucoma, and diabetic retinopathy because the State agencies had consistently reported that these were the leading causes of adult blindness in the U.S.

When the Framingham Eye Study began, the age of the study population ranged from 52 to 85 years, the time of life during which these diseases occur most frequently.

The most important findings are:

- Framingham residents with *senile cataract* were found more likely to have increased levels of a type of blood fat (serum phospholipid), high nonfasting blood sugar levels, and high blood pressure.

Associations with aging-related factors were also found, as expected. Only diabetes has been previously reported as a risk factor for senile cataract.

Prevalence of cataract for both sexes was almost 5 percent for ages 52-64, 18 percent for those aged 65-74, and 46 percent for the 75-85 age group.

- Persons with *senile macular degeneration* showed a positive association with increased blood pressure, enlarged left side of the heart (ventricular hypertrophy), a history of lung infection, and aging-related factors.

Macular degeneration was also more common among women than men.

Prevalence of macular degenera-

NIH Visiting Scientists Program Participants

7/22—Dr. Masanobu Ohashi, Japan, Reproduction Research Branch. Sponsor: Dr. Hao-Chia Chen, NICHD, Auburn Bg., Rm. 210.

7/28—Dr. John S. Harington, S. Africa, Research Resources Program. Sponsor: Dr. John A. Moore, NIEHS, Research Triangle Park, N.C.

8/1—Dr. Soraya Naghshineh, Iran, Laboratory of Chemistry. Sponsor: Dr. Louis Cohen, NIA-MDD, Bg. 4, Rm. 328.

8/8—Dr. Reuven Laskov, Israel, Laboratory of Microbial Immunity. Sponsor: Dr. Richard Asofsky, NIAID, Bg. 5, Rm. 235.

8/10—Dr. Suguru Fukushi, Japan, Laboratory of Vision Research. Sponsor: Dr. Jin Kinoshita, NEI, Bg. 6, Rm. 222A.

8/14—Dr. Ernest Winocour, Israel, Laboratory of Biochemistry. Sponsors: Drs. Edward Kuff and Maxine Singer, NCI, Bg. 37, Rm. 4C03.

8/18—Dr. Dileep Deobagkar, India, Laboratory of RNA Tumor Viruses. Sponsor: Dr. John Stephenson, NCI, Frederick Cancer Research Center.

8/21—Dr. James L. Hill, Canada, Laboratory of Brain Evolution and Behavior. Sponsor: Dr. John B. Calhoun, NIMH, Bg. 112, Poolesville.

8/22—Dr. Noveen Das, Pakistan, Laboratory of Vision Research. Sponsor: Dr. Hitoshi Shichi, NEI, Bg. 6, Rm. 214.

8/22—Dr. Yu-Ching Pan, Taiwan, Laboratory of Environmental Mutagenesis. Sponsor: Dr. Joseph Marciniak, NIEHS, Research Triangle Park, N.C.

8/25—Dr. Tomomi Oishi, Japan, Clinical Investigations Branch. Sponsor: Dr. Richard Webber, NIDR, Bg. 10, Rm. 2B09.

tion for both sexes was 2 percent for those aged 52-64, 11 percent for those aged 65-74, and 28 percent for the 75-85 age group.

Mr. Kahn and Dr. Leibowitz hope that further study of their preliminary findings will ultimately provide clues to the causes of eye disease just as the well-known Framingham Heart Study first identified major risk factors for coronary disease.

Findings Are Preliminary

They caution that the Eye Study's preliminary findings may be a mix of real and chance associations, and therefore emphasize that these results may be replicated in an independent population before they can be considered as risk factors for eye disease.

Mr. Kahn, Dr. Leibowitz, and their associates published their findings in the August issue of the *American Journal of Epidemiology*.

NICHD Researchers Find Birth Defects, Aromatic Hydrocarbon Response Linked

A recently discovered genetic system, enabling the body to be protected from drug and other foreign substance poisoning, may render some individuals susceptible to birth defects. This is a finding of National Institute of Child Health and Human Development scientists working with Dr. Daniel Nebert, chief of the Developmental Pharmacology Branch.

According to Drs. Nebert, Shu Shum, and George Lambert, offspring of pregnant mice treated with poisonous chemicals called polycyclic hydrocarbons differ in their ability to metabolize them.

Conversion Results in Damage

Fetuses converting the toxicants into a different form are far more likely to be deformed, stunted, or killed than fetuses metabolizing the chemicals less efficiently.

In the strains of mice studied, the individual mouse's capacity to metabolize hydrocarbons is determined by a genetic system, the "aromatic hydrocarbon responsiveness locus."

The *Ah* locus, discovered by Dr. Nebert and his co-workers more than 6 years ago, is present in many animal cells, including man. It consists of one gene or a small number of genes which control the body's capacity to rid itself of numerous toxic substances.

Among these are hydrocarbons in cigarette smoke, charcoal-broiled foods, and automobile exhaust fumes. Other chemicals whose fate is determined by the *Ah* locus include fat-soluble compounds used as drugs, insecticides, and raw materials for industry.

If allowed to accumulate in the tissues, many of these substances are poisonous and may cause cancer, mutations, or birth defects. When one of the toxicants enters a cell, the *Ah* locus in the cell's nucleus is activated in some as yet unknown manner.

Activation of the *Ah* locus boosts the activity of a series of enzymes called monooxygenases. These enzymes modify the original toxic chemical into a new substance which can be attacked and further degraded by another set of enzymes called conjugating enzymes. The final product will be a harmless substance which can be excreted from the cell and from the body.

Individuals Differ

Individual humans and various strains of laboratory mice differ in their enzymatic response to hydrocarbons. In mice having a "responsive" form of the gene(s) at the *Ah* locus, hydrocarbon exposure brings about a dramatic rise in monooxygenase enzyme activity.

In other mice, called "nonresponsive," the increase does not occur at all in the liver and is small in all tissues other than liver. When a responsive mouse is mated with a nonresponsive mouse, the offspring

are usually responsive. Genetically, it can be said that aromatic hydrocarbon responsiveness in mice, like brown eye color in humans, is inherited as an autosomal dominant trait.

Through a series of crosses between genetically responsive and genetically nonresponsive mice, Drs. Shum and Nebert studied pregnancies in which fetuses of both genetic types were present in the same womb. In this situation, early exposure of the pregnant mouse to a polycyclic hydrocarbon causes massive damage to fetuses with the responsive gene(s) at the *Ah* locus.

Malformations Observed

About 75 percent of these fetuses are deformed or killed, and virtually all the survivors are growth retarded. In contrast, their nonresponsive littermates suffer fewer malformations, only a slight growth inhibition, and a much lower death rate.

Malformations observed in this study include cleft palate, club foot, absence of an eye, nose and jaw underdevelopment, kidney or liver abnormalities, and heart protrusion outside of the body cavity.

Suggest Link With Smoking

This study proves that genetic factors within fetal tissues can determine fetal susceptibility to birth defects when the baby in the womb is exposed to chemicals by way of the mother.

Results also suggest a possible explanation for the low birth weight of human infants whose mothers smoked cigarettes during pregnancy. It seems likely that this form of intrauterine growth retardation may be caused by hydrocarbons "triggering" the *Ah* locus.

Responsiveness Aids Adults

For an adult animal receiving hydrocarbons in its food, having the responsive form of the gene(s) at the *Ah* locus can be of considerable survival value. This trait enables the animal to dispose of the hydrocarbons more efficiently. However, for the embryo or fetus exposed to hydrocarbons at a critical point in its development, the responsive form of the gene is a liability.

This apparent contradiction can be explained partially by earlier studies showing that the first products of monooxygenase activity are highly reactive compounds.



Dr. Nebert and his colleagues believe their work may be useful in explaining individual susceptibility to birth defects, degenerative diseases, poisoning by environmental chemicals, and environmentally-caused types of cancer.

They can damage the cell's genetic material if not detoxified immediately.

Apparently, fetuses genetically responsive to hydrocarbons may form these dangerous intermediates in sufficient quantity to cause irreparable damage to their tissues. The nonresponsive fetuses seem to be protected by their inefficiency in coping with hydrocarbons.

Responsive Fetus Is Vulnerable

Another possible explanation for vulnerability of the responsive fetuses is that these monooxygenases are capable of metabolizing hormones normally in the body as well as foreign chemicals. When monooxygenase activities are prematurely "triggered" by a foreign hydrocarbon, the fetus may break down hormones needed for normal growth and development.

This mechanism could explain the high incidence of low birth weight observed in the responsive fetuses.

Laboratories around the world

SCREENING

(Continued from Page 1)

data from the 1960's Health Insurance Plan (HIP) Study of Greater New York and the possible risks for breast cancer from exposure to ionizing radiation.

The panel also will consider a new report to be received from a working group studying data from the Breast Cancer Detection Demonstration Project. This screening project is cosponsored by NCI and the American Cancer Society.

All sessions are open to the public.

are now attempting to apply *Ah* locus information to the prevention of human disease. A search is underway to identify human groups or individuals whose *Ah* responsiveness places them at risk for diseases caused by environmental chemicals.

NICHD researchers are collaborating with National Eye Institute investigators to determine whether the *Ah* locus plays a role in causing cataracts to form in response to certain drugs and in causing retinitis pigmentosa, a degenerative disease of the eye.

Current NICHD studies aim at a more detailed understanding of the monooxygenase enzymes and the genetic control mechanisms enabling the *Ah* locus to respond to hydrocarbons.

Note Interaction

In the exploratory phase, the group's work has already begun illuminating one of the most mysterious areas of human biology—the area of gene-environment interaction. From their work and other scientists' work, it may someday be possible to detail how a specific gene and a specific environmental pollutant act together at the cellular level causing death, disease, and disability.



The NCI Office of Program Planning and Analysis staff recently received a group award for superior performance in carrying out their activities in planning, analysis, management, budget forecasting, and information systems. Receiving the award were (standing l to r): Michael Brown, Dr. Michael Klein, Dr. Abraham Cantarow, Dr. Vaman Waravdekar, Florence Livingston, Jack McShulskis, Barbara Murray, Joseph Sberro, Douglas Pugh, Carole Maloney, Sheila Morris, Dr. Robert Love, Dr. Elliott Stonehill, and Joanna Papa. Seated (l to r) are: Christine Hauptman, Louis Carrese, associate director, OPPIA, who recommended the group for the award, Dr. Guy R. Newell, then acting Director of NCI who presented the awards, Ora Bynum, Betty Ann Sullivan, and Joseph Bongiolo. Not shown: Jacqueline Parkham and Dr. Daniel Rubin.

Sex Life of Gonococci Spreads Penicillin Resistance, Seattle NIAID Grantees Say

The sex life of the gonococci—the bacteria causing human venereal disease—may itself provide clues as to how and why penicillin-resistant strains of the organism have recently appeared in various parts of the world.

This finding, by NIAID grantees at the University of Washington, Seattle, has serious implications not only for the control of gonorrhea but also for other diseases, such as meningitis, caused by related but currently penicillin-sensitive organisms.

Transfer Methods Described

In bacteria, transfer of hereditary information may take place in a variety of ways. For example, transformation involves the absorption by a bacterial cell of DNA (deoxyribonucleic acid) chemically extracted from a donor cell.

In contrast, conjugation consists of the transfer of genetic material as a consequence of cellular contact between sexually differentiated bacteria.

The sex of a bacterial strain depends upon the presence (male) or absence (female) of a genetic structure known as the sex factor.

Of all phenomena of genetic transfer in bacteria, conjugation is the one which most closely resembles the sexual pattern of higher forms of life.

Earlier work by the Seattle investigators showed that the ability of gonococci to make a penicillin-destroying enzyme (β -lactamase), thus becoming completely resistant to the ordinarily curative drug, was transferred from one strain to another by circular bits of DNA known as plasmids.

In studying β -lactamase-producing gonococci from the Far East, Drs. Marilyn Roberts and Stanley Falkow noted that the bacteria differed in so many ways that it seemed unlikely that they all arose from a single ancestral resistant strain.

For this reason, the scientists investigated the possibility that the gonococcal R (for resistance) plasmid DNA could have been disseminated by transformation—historically the only known mode of genetic transfer among gonococci and related species.

Transformation Not Responsible

Drs. Roberts and Falkow found, however, that the gonococci were refractory to transformation by closed circular plasmid DNA and, therefore, that dissemination of the gonococcal R plasmids was not likely to be through transformation.

In a second set of mating experiments to examine the conjugative properties of gonococci, β -lactamase-producing strains were used as the donors (males) and the recipient (female) strain was a non- β -lactamase producer.

The investigators found that successful transfer of the R plasmid

was observed only when the donor gonococci contained a second large indigenous plasmid.

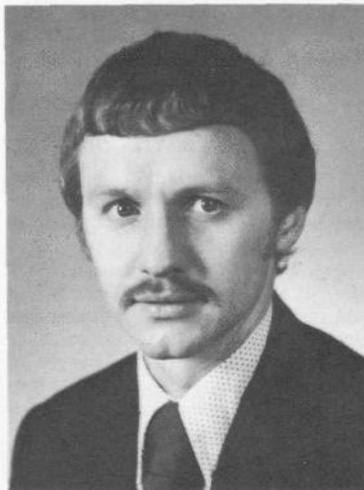
This plasmid was assumed to have "sex factor" activity and through conjugation to promote the transfer of the smaller co-existing R plasmid.

Furthermore, it was found that in overnight mating experiments, considerable numbers of gonococcal recipients received the large "sex factor" plasmid along with the R plasmid and thus became capable of passing along the latter.

R Plasmids Transmitted

In view of the ease with which R plasmids can seemingly be transmitted among various strains of gonococci, the investigators express concern that through the process of conjugation other related bacterial species presently penicillin-sensitive may also become β -lactamase producers and therefore resistant to penicillin or penicillin-based antibiotics.

A report on this work, and an accompanying editorial, appeared in the April 14 issue of *Nature*.



Dr. Curis D. Klaassen, department of pharmacology, University of Kansas Medical School, was recently awarded the 1976 Achievement Award of the Society of Toxicology—given for outstanding contributions in toxicology by a young scientist less than 36 years of age. Dr. Klaassen is a participant in the Medical School's NIGMS-supported Pharmacology and Toxicology Center, where his award-winning research on the biliary excretion of drugs and toxic compounds was conducted. He also is a member of the DRG Toxicology Study Section.

Seattle Researchers Find Sex Matching Aids Bone Marrow Transplant Outcome

The occurrence of Graft Versus Host Disease (GVHD) and survival of patients with aplastic anemia treated by bone marrow transplantation are strongly influenced by the sex match of the marrow donor and recipient. This is the major finding of NIAID-sponsored researchers at the University of Washington and Fred Hutchinson Cancer Research

Center in Seattle, Wash., who reviewed the records of more than 70 aplastic anemia patients who were bone marrow recipients.

Recent studies have indicated that grafting marrow from an HLA identical sibling is more effective than conventional therapy for the treatment of severe aplastic anemia.

However, high mortality is still associated with this procedure and can largely be accounted for by marrow graft rejection and GVHD.

Two Factors Associated

The Seattle researchers have been concerned with both of these phenomena. In other investigations, they have found marrow graft rejection to be associated with two prognostic factors: positive *in vitro* tests of sensitization of marrow recipient against marrow donor and a low number of marrow cells used for transplantation.

The present analysis was aimed at identifying prognostic factors associated with GVHD and survival of those patients who did not reject their marrow graft, but rather showed sustained marrow engraftment.

Of 73 consecutive patients with severe aplastic anemia treated by marrow transplantation from HLA identical siblings, five patients died within 8 days following transplantation, too early for meaningful evaluation.

In addition, 21 patients rejected their initial graft, and only two of them survived. In contrast, the scientists reported there were only 18 deaths among 47 patients who had sustained engraftment. In 16 of these patients, death was associated with GVDH.

Study Sustained Engraftment

Twenty-nine of the 47 patients with sustained engraftment were alive with complete hemologic restoration between 8 months and 5 years at the time this study was reported.

Since GVHD was obviously not a problem in patients with graft rejection, the scientists felt that it was reasonable to focus analysis in this study on the group with sustained engraftment.

The Seattle researchers used statistical methods to analyze the pre- and post-transplantation data in order to identify factors that predicted survival.

Of the 24 factors entered into the analysis, only two strongly correlated with survival: (a) sex

match of the donor and recipient and (b) absence of refractoriness (unresponsiveness) to random donor platelets at the time of transplantation.

However, refractoriness adversely influenced only the survival of the sex mismatched patients.

According to the scientists, this data suggests that X and Y associated transplantation antigen systems are important determinants of the outcome of marrow grafts between HLA identical siblings for the treatment of aplastic anemia.

However, they stress that these findings are based on data involving a rather small sample size (47 patients, 18 deaths) and that factors such as preceding androgen treatment and age should be more closely monitored in future studies. In addition, the mechanisms by which refractoriness to random donor platelets influences survival are currently unclear.

If confirmed, these findings have some obvious therapeutic implications, e.g. selection of a sex matched marrow donor if several HLA identical siblings are available, and early transplantation (a) because of the excellent chances for survival in the case of a sex matched recipient, and (b) to prevent further deterioration of the chances for survival in the case of a sex mismatched recipient by avoiding the development of refractoriness.

May Develop Detection

In addition, the Seattle scientists believe that knowledge of the association of antigens important for the development of GVHD and the X and Y chromosomes in man might lead to the development of *in vitro* typing techniques to detect these antigens.

Availability of such typing techniques will facilitate the selection of donor recipient pairs for marrow transplantation in aplastic anemia.

This study was reported in the April 1977 issue of *The Journal of Clinical Investigation* by Drs. Rainer Storb, Ross L. Prentice, and E. Donnall Thomas.

Women Golfers Meet Sept. 15

The next meeting of the NIH Women's Golf Association will be held on Thursday, Sept. 15, at 7:30 p.m. in the Bldg. 1 Cafeteria (3rd floor).

Election winners will be announced, and plans for the 1978 season discussed.

Look at Hypertension Opens Weekly Series, Medicine for Layman

The Clinical Center invites NIH employees, their families, and friends to boost their health I.Q.'s at a weekly series of seminars entitled *Medicine for the Layman*.

The series begins Tuesday, Sept. 20, at 8 p.m. in the Masur Auditorium with a look at the problem of hypertension.

Dr. Harry Keiser, clinical director of the National Heart, Lung, and Blood Institute, will examine the highs and lows of the problem, including its causes, its effects on the body, and recent advances in treating the disorder.

Each hour-long presentation will be accentuated by colorful and entertaining illustrations designed by noted local artists.

On Sept. 27, Dr. Robert Butler, Director, National Institute on Aging, and winner of a Pulitzer Prize for his book, *Why Survive? Growing Old in America*, will discuss the biological processes of aging and current research in that area.

Diabetes is the topic for Oct. 4. Dr. Jesse Roth, chief of the Diabetes Branch, National Institute of Arthritis, Metabolism, and Digestive Diseases, will speak on the different types of diabetes, clues to help detect the disease, complications, and treatment for diabetics.

Will Discuss Hormone Levels

CC Director Dr. Mortimer Lipsett will discuss the menstrual cycle and fertility on Oct. 11. Part of his talk will deal with the significance of hormone level changes as they relate to menses, oral contraceptives, conception, and menopause.

The lectures will be held every Tuesday evening at 8 p.m. (except Nov. 8) and will continue through Dec. 13.

Other topics scheduled later in the series include: Immunity, Oct. 18; *The Heart: Diagnosis and Treatment*, Oct. 25; Heart Attacks, Nov. 1; The Brain, Nov. 15; Obesity and Energy Metabolism, Nov. 22; The Lungs, Nov. 29; Cancer: What Is It?, Dec. 6; and Cancer Treatment, Dec. 13.

Graduate School Registration For Fall Will Begin Tomorrow

Evening courses for the fall semester of the Graduate School at NIH begin Monday, Sept. 19.

The Graduate School is sponsored by the Foundation for Advanced Education in the Sciences.

Registration starts tomorrow, Sept. 8, through Sept. 14 in the Clinical Center, Room B1-L-101.

For a catalog or further information, call Ext. 65272.

Series on Mental Retardation Published: Results of 12 NICHD-Supported Centers



The NICHD book series represents the work of the entire MRDDB staff, (standing l to r) Drs. Theodore D. Tjossem, Felix de la Cruz, Lyle Lloyd, Michael J. Begab, and (seated l to r) Evonne Williams, Faith VanScoyoc, and Mary Kern.

The Mentally Retarded and Society: A Social Science Perspective, part of the National Institute of Child Health and Human Development Mental Retardation Research Center Series, was termed "a new milestone" in a book review in the June 10 issue of *Science* magazine.

A major portion of this book pertains to the treatment of retarded individuals including mainstreaming, deinstitutionalization, normalization, foster family care, and vocational training.

It includes chapters on general communication problems, attitude change, compensatory education, and the treatment of juvenile delinquency.

The 8-book series is the result of a state-of-the-art conference planned jointly by the NICHD and its 12 mental retardation research centers.

The centers, located at geographically dispersed universities, differ considerably from each other in the breadth and depth of their research emphases.

Centers Described

Most of the centers are multidisciplinary, embracing biological, behavioral, and clinical research. Some are more narrowly focused on biomedical science while others are primarily behavioral in their approach. As a unit, the centers are an extensive effort reflecting the complexity of the mental retardation problem.

Accordingly, the series reflects the complexity of the problem and includes articles on basic and applied research; an extensive bibliography is part of each book.

Dr. Michael J. Begab, head of NICHD's Mental Retardation Research Centers Program and co-editor of the reviewed book, said the series has many uses in addition to archival value.

Together, the books provide new investigators, practitioners, and

students a current and encyclopedic view of the field and highlight promising directions for future research.

The series aids communication among the field's diverse workers, he said, and informs the public of how research efforts guide and assist those affected by retardation, social policy-makers, and community planners.

For example, *Language of the Mentally Retarded*, prepared by the NICHD and the University of Kansas Center, is the result of multidisciplinary collaborative research.

Contributors include scientists, speech clinicians, audiologists, special educators, linguists, psychologists, and others.

Dr. Theodore D. Tjossem, chief of NICHD's Mental Retardation and Developmental Disabilities Branch, the organizational unit for the research centers program, edited another of the series, *Intervention Strategies for High Risk Infants and Young Children*.

Refers to Early Efforts

This publication refers to early efforts and techniques to maximize development of children at risk for aberrant development. It reports on new advances in research, service, and training of these children and their caretakers.

One chapter, "Pediatric Care and Training: A Paradox?" reviews the pediatrician's role in caring for infants with cognitive and language deficiencies. The contribution is authored by Dr. Felix F. de la Cruz, special assistant for pedi-

DRR Issues Directory Of Its Animal Resources As Guide to Scientists

A 56-page directory describing the animal resources of the Division of Research Resources has been published and is available at no charge.

Titled *Animal Resources, A Research Resources Directory*, the booklet is intended as a guide to scientists seeking resource assistance and collaboration involving animals in biomedical research.

In addition to the complete listing of NIH's major Primate Research Centers, the directory identifies animal diagnostic laboratories, animal information projects, animal reference centers, and special colony and model study centers currently supported by DRR.

The Directory indicates the services provided, areas of research interest, principal investigators or directors, addresses, and telephone numbers. A contact person is identified for each resource.

A geographic index is included, listing resources by state, and within each state. A map shows the locations of the Primate Research Centers and animal laboratories throughout the country.

A single free copy of *Animal Resources, A Research Resources Directory* may be secured by writing to the Research Resources Information Center, 1776 East Jefferson St., Rockville, Md. 20852, or by request from the Office of Science and Health Reports, Division of Research Resources, NIH, Bethesda, Md.

atrices in NICHD's MRDDB.

Other articles include caregiver/infant interaction, the infant's auditory environment, trends in behavioral research, and international perspectives.

The book is a reference for educators, therapists, clinicians, and researchers as well as nonprofessionals involved with the care and treatment of developmentally disabled children.

Others in Series Listed

Other books in the series are *Brain Mechanisms in Mental Retardation*, *Methodological Approaches to the Study of Brain Maturation and Its Abnormalities*, and *Antenatal Diagnosis*.

Soon to be released is *Communicative and Cognitive Abilities—Early Behavioral Assessment*, edited by Dr. Lyle Lloyd, Health Scientist Administrator for the MRDDB. Another report titled *Observing Behavior, Volumes I and II* is also in press.

Additional information on the books may be obtained from Dr. Begab, NICHD, Landow Bldg., Room C708, 7910 Woodmont Ave., Bethesda, Md. 20014 (301-496-1383).