Dr. Albert Sabin Joins FIC; Developed Oral Polio Vaccine

Dr. Albert B. Sabin, developer of the oral polio vaccine, was recently appointed as an FIC Senior Expert Consultant by Dr. Craig K. Wallace, Director of the Fogarty International Center. Dr. Sabin's wide experience in the international aspects of biomedical research will be an invaluable asset to the Fogarty Center programs.

He will be working most closely with the International Studies Branch in its efforts directed at the control and eradication of diseases, specifically, in its follow-up to the March 1982 International Symposium on Measles Immunization and the March 1983 International Symposium on Poliomyelitis Control.

He will also assist the branch in developing its long-term collaborative programs with the World Health Organization in this area. His arrival at FIC is an important milestone in the Fogarty International Center's development of the advanced studies program.

Dr. Sabin was born in Russia (now Poland) in 1906. He was graduated from Paterson (N.J.) High School in 1923 and from New York University, where he received his M.D. degree in 1931. He had a long and distinguished career (spanning five decades) at the Lister Institute (England), Rockefeller Institute (New York), University of Cincinnati College of Medicine, as President of The Weizmann Institute of Science (Israel), and at the Medical University of South Carolina.

Ancient Hindu Remedy From Coleus Plant Stimulates Enzymes, NIADDK Scientists Find

By Linda Stalvey

An ancient Hindu folk remedy has piqued the interest of modern scientists, becoming an invaluable research tool and perhaps a multifaceted therapeutic agent.

Ancient Hindu and Ayurvedic texts describe the use of a species of Coleus plant as a remedy for such varied ailments as heart disease, stomach aches, respiratory disorders, and insomnia. A particular species, Coleus forskohlii, is still used in Indian folk medicine today.

Named for the Swedish naturalist, Pehr Forskal, who was a student of the famed Carolus Linnaeus, and who died of thirst in the desert after his packers deserted him, Coleus forskohlii has brought belated recognition to its ill-fated namesake.

Extracts from the roots of the plant were found to have marked effects as a cardiac stimulant and as a muscle relaxant. The active principle was isolated by chemists at Hoechst Pharmaceuticals Ltd. Bombay, India, its structure determined and the name forskolin given to it.

Dr. John W. Daly, chief, Laboratory of Biological Chemistry, National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases, noted for his work with natural products, was asked to examine possible mechanisms involved in the action of forskolin.

A Note to the NIH Community

Camp Fantastic and the NIH R&W Association would like to thank the employees of the NIH for their continued support of Camp Fantastic, a camp for children with cancer. During the recent "2nd Annual R&W Camp Fantastic Barbecue," many people patiently stood in a very long line awaiting the very late arrival of the caterer.

Fortunately, pleasant weather, comic gestures by Dr. Mary Medicine and Dr. Marty Frank and expert juggling by a mystery juggler saved the day. During the past 3 months, NIH supporters have donated over $2,600 to Camp Fantastic, an amount that will send 10 children with cancer to Front Royal, Va. for a week of fun and laughter.

Your continued support along with your patience at the Barbecue is sincerely appreciated.

This initial work with forskolin, published by Dr. Daly and his colleagues Dr. Kenneth Seamon and William Padgett in June of 1981, delineated the substance's mechanism of action. This basic research has, in a few short years, stimulated hundreds of subsequent papers.

The discovery, which so excited the biomedical research community, was that forskolin had a unique effect on the enzyme adenylate cyclase. Adenylate cyclase is found in the membranes of cells throughout the body. It is a key enzyme for the control and regulation of various cellular processes and is an integral step in the action of many hormones.

To initiate a specific cellular response, a hormone must first bind to a receptor on that cell's membrane. The adenylate cyclase, located in the cell membrane, is stimulated by the binding of the hormone to its receptor to produce, through a biochemical reaction, a substance called cyclic AMP.

Cyclic AMP, known as a second messenger (for it continues the message of the hormone), initiates another set of biochemical reactions within the cell that ultimately results in a specific response.

The research of Drs. Daly and Seamon showed that forskolin stimulates adenylate cyclase.

(See FORSKOLIN, Page 12)
Egyptian, Israeli Scientists Work Together on Malaria Research

An Egyptian and an Israeli scientist have come to NIAID’s Laboratory of Parasitic Diseases (LPD) for the first time to work side-by-side on malaria research as part of the 1983 Cooperative Research Project on arthropod-borne diseases between the United States, Egypt, and Israel.

Dr. Rachel Galun, currently on sabatical from LPD, will return in October to the Kuvim Center for the Study of Infectious Diseases at Hebrew University, Jerusalem. She is Israel’s principal investigator on this cooperative agreement and LPD’s Dr. Robert Gwadz is its principal scientific advisor.

Ms. Shoukry, a graduate student, will return to Ain Shams University in Cairo upon completion of her work at LPD and at the Boyce Thompson Institute for Plant Research at Cornell University, N.Y.

New Pamphlet Explains Body’s Immune System

Because the immune system is a key aspect of both health and disease, the National Institute of Allergy and Infectious Diseases has produced a new pamphlet, Understanding the Immune System.

Not so many decades ago even scientists had little knowledge of the immune system. Physicians had observed, since antiquity, that many infections such as measles and other childhood diseases stimulated lifelong immunity to reinfection.

Once it was understood that microbes were responsible for both infection and immunity, it was only a matter of time before scientists developed vaccinations to produce this same immunity.

Protection a Mystery

Exactly how this remarkable protection came about remained a mystery. It was a mystery in 1796 when Edward Jenner introduced vaccination for smallpox, and it was still largely a mystery when Jonas Salk and Albert Sabin introduced the polio vaccines of the 1950s.

But this is rapidly changing. Scientists are now learning the roles played by each component of the complex network of organs and cells that make up the immune system. They are learning, too, that this extraordinary system not only prevents but may also cause disease.

A malfunctioning immune system is responsible for many common allergies such as asthma and hayfever, and for a large number of autoimmune diseases such as systemic lupus erythematosus.

Immune Deficiency

Now the current epidemic of Acquired Immune Deficiency Syndrome (AIDS) has brought widespread attention to another class of immune disorders—immn deiciency diseases.

These diseases occur when one or more parts of the immune system is missing or does not function properly, subjecting the body to unrepeled invasion by hundreds of microbes.

There is also growing evidence that the immune system is linked to the development of many chronic diseases such as cancer, rheumatoid arthritis and multiple sclerosis.

For single copies of “Understanding the Immune System,” write to “Immune/H.I.” Information Office, National Institute of Allergy and Infectious Diseases, Bldg. 31, Rm. 7A32, Bethesda, MD 20205; or call (301) 496-5717. — Nancy Brun

Camp Fantastic

Camp Fantastic, which will be held Aug. 19-26 this year, is a week-long summer camp for children undergoing cancer treatment.

Sponsored by Special Love, Inc. (a non-profit organization) and staffed by NIH volunteers, the camp will provide meaningful experiences for these children who fight against cancer every day of their lives. For more information, call the R&W Activities Desk at 496-6061. □
NIADDK Summer Student Wins Award for Science Paper

Kimberly D. Kenward, a summer employee of the National Institute of Arthritis, Diabetes and Digestive and Kidney Diseases, won honorable mention in the Washington area 1984 high school science writing contest awards for her paper entitled "From the Bloodstream Into the Cell: A Lipid Movement Theory."

The awards are sponsored by the Society for Technical Communications to encourage "clear writing about complex matters...[and] for development of competence in communicating facts and ideas."

Ms. Kenward, a June graduate of Walter Johnson High School, Bethesda, spent last school year working with Dr. Robert O. Scow, chief, Endocrinology Section, Laboratory of Cellular and Developmental Biology, NIADDK. She worked as a biomedical intern in a special program offered by Walter Johnson High School in collaboration with several individual scientists at NIH.

This highly technical and specialized career-oriented program for the intellectually gifted student provides on-the-job training and exposure to the research laboratory. Students are evaluated by their NIH supervisor and a Walter Johnson High School science advisor, and prepare a written report about their laboratory experiences. In return the interns gain high school credit.

Study Shows Diet Can Affect Sleep Stages in Newborns

The composition of a newborn's diet can influence the amount of time it takes the infant to fall asleep after a feeding, according to a recent study supported in part by the National Institute of Child Health and Human Development.

Researchers at Harvard Medical School and Boston University School of Medicine have found that the stages in a newborn's sleep pattern can be affected by two amino acids—tryptophan and valine.

Twenty healthy, bottle-fed newborns (2-3 days old) were involved in the study. One of the infant's evening feedings was replaced by a commercial formula feeding. The onset of active and quiet sleep stages in the newborns fed the valine solution took 14 minutes earlier and the quiet sleep stage 20 minutes earlier than after a regular infant formula feeding.

Newborns go through several sleep stages that can be measured by their behavior. Typically, a newborn enters sleep through active sleep, a period of rapid eye movement, frequent body movements and irregular respiration.

This stage is followed by quiet sleep where the infant's eye movements are no longer visible, respiration is regular and body movements are minimal.

The third stage is a combination of quiet and active sleep. The other stages include drowsiness, wakefulness and fretting or crying.

Tryptophan is essential for the synthesis and release of serotonin, a neurotransmitter in the brain which is believed to be partially responsible for regulating sleep behavior in humans. Tryptophan is found in breast milk and infant formulas, as well as in high protein foods like milk, poultry, and eggs.

The amount of tryptophan and valine delivered to the brain is affected by the concentration of these amino acids in the blood. Valine and tryptophan compete for the same carrier mechanism that allows their entry into the brain. Therefore, the valine will monopolize the carrier and decrease the amount of tryptophan transported into the brain.

The researchers, Drs. Michael Yogman and Steven Zeisel, say this study demonstrates that the onset of newborn sleep stages can be influenced by diet without disrupting the normal pattern of falling asleep.

Although adults and newborns have different sleep pattern organizations (adults enter sleep through the quiet stage), similar effects on the onset of sleep have been produced in adults by modifying dietary components, according to the researchers.

They said past research on nutrition and infant behavior has focused on long-term effects. This study examined the short-term effects of modifying only a single component of the diet on newborn sleep behavior.

This study was reported in The New England Journal of Medicine, Vol. 309, No. 19.

Volunteers Wanted for NIA Study

The laboratory of neurosciences of the National Institute on Aging is seeking adult volunteers in good health, between the ages of 30 to 70 years for a study of cerebrospinal fluid. This will involve a screening physical examination and a lumbar puncture. Volunteers will be paid.

Interested persons should call Dr. Conrad May, 496-4754.

NIH Chamber Music Association Seeks New Member Applicants

The R&W NIH Chamber Music Association is accepting applications for membership. The association is an organization which fosters the joining together of chamber music players who enjoy reading or rehearsing the vast repertoire for such groups. The membership list is distributed to all members.

The association also sponsors the R&W NIH Chamber Orchestra which will begin its third season in the fall under conductor David Crane. The orchestra of approximately 35 string and woodwind players performs three concerts each season in the Clinical Center's Masur auditorium for the NIH community, family, friends, and neighbors.

To join the R&W NIH Chamber Music Association, or for further details, contact Nannette R. Melnick at 496-8768 or Dr. John B. Wolff at 496-7070. A 1984 R&W Association membership card is required.

Nothing is more unpleasant than a virtuous person with a mean mind.—Walter Bagehot

DR. SABIN

(Continued from Page 1)

(Charleston). He served in the U.S. Army from 1943 to 1946.

From 1947 to 1973, he was a consultant to the U.S. Public Health Service (NIH), and he was a member of the National Advisory Council of NIADDK from 1965 to 1970.

In 1973, he was selected as a Fogarty Scholar-in-Residence. In 1974, he was an expert consultant with NCI, and from 1975 to 1977, he was a consultant to the Assistant Secretary for Health.
Chickenpox Vaccine Protects Children With Leukemia

Results of a collaborative study on the effectiveness of the varicella virus vaccine against chickenpox in children with leukemia was recently reported in the July 20, 1984, Journal of the American Medical Association by National Institute of Allergy and Infectious Diseases-supported scientists.

Chickenpox, caused by the varicella-zoster virus, affects thousands of Americans each year, usually children between the ages of 5 and 10. Usually the disease is mild, and complications are rare. However, for children with suppressed immune systems such as those with leukemia and undergoing chemotherapy, chickenpox can be a severe, complicated, and sometimes fatal disease. One study showed that 30 percent of these children developed disseminated disease, in which the varicella virus affects organs throughout the body. Seven percent of the children died.

The only control measure presently available to prevent chickenpox is passive immunization, that is administration of concentrated antibodies derived from the blood of persons who have had the natural infection. This product, called varicella-zoster immune globulin (VZIG), is somewhat effective in preventing disease if given within 72 hours of exposure to the virus.

In the 1970s Japanese scientists developed a varicella vaccine using attenuated (weakened) live virus. Their studies showed that it was safe for normal and immunocompromised children and that it would stimulate antibodies like those induced by the natural infection. However, further studies were necessary to carefully measure the reactions of at-risk, leukemic children on chemotherapy.

Dr. Anne A. Gershon, New York University Medical Center, has recently reported the results of a comprehensive collaborative study to determine the effectiveness of varicella vaccine, prepared from the Japanese Oka strain, in protecting at-risk children. The study was supported by a contract from NIAD.

Dr. Gershon and her colleagues at hospitals throughout the United States immunized—over a 3-year-period—a total of 191 children who had acute leukemia. All had been in remission for at least 1 year, approximately two-thirds were receiving maintenance chemotherapy, and all were susceptible to chickenpox.

The live, attenuated varicella vaccine effectively prevented severe chickenpox in all vaccinated children. There was no evidence that vaccination increased the risk of relapse of leukemia.

Blood tests showed an immune response to the vaccine in 82 percent of the children after one dose, and in 95 percent after a second dose. No severe side effects were noted. Some children did have mild reactions, but in no case was treatment required. These children generally developed the higher antibody levels.

Careful observation showed that there is some risk (about 10 percent) that children with vaccine-associated reactions can transmit the vaccine virus to susceptible household contacts, causing them to have mild infections.

Twenty-two of the vaccinated children were later exposed to the natural, wild-type virus in their households. Most were protected, but 18 percent did develop mild cases of chickenpox, despite the fact that their immune systems had responded to the vaccine.

Dr. Gershon and her colleagues speculate that some immunosuppressed patients may have subtle defects in certain immune responses that predispose them to clinical infection with the wild-type virus after a natural exposure.

Fortunately, the disease in these children was extremely mild, much milder than the illness that occurs in children who are exposed to unattenuated virus. The 18 percent attack rate was also much less than the 80 to 90 percent attack rate in normal susceptible children with household exposure to the wild-type virus.

Several of the vaccinees who developed mild infections did not realize that they had been exposed to varicella virus and would not have been given VZIG. Without active immunization with the vaccine, they probably would have developed severe infections.

Dr. Gershon concludes, "While it does not provide total protection from disease in immunocompromised children, live attenuated varicella vaccine is safe and effective. It should provide relief from fear of severe chickenpox in children with leukemia."

Authors of the report are Dr. Gershon and Sharon Steinberg, New York University Medical Center; Dr. George B. Bassford, NIAD; Dr. William Borkowsky, Philip LaRussa, Angelo Ferrara, Lawrence Gelb, and the NIAD Varicella Vaccine Collaborative Study Group.

Visiting Scientist Program Participants

Sponsored by Fogarty International Center

[List of participants]

Stanley I. Rapport, Laboratory of Neurosciences, NIA, 10, Rm. 6C103.
6/5 Dr. Hirohisa Kurachi, Japan. Sponsor: Dr. Takami Oka, Laboratory of Biochemistry and Molecular Biology, NINDD, 10, Rm. 8S09.
6/6 Dr. Kazuto Shigematsu, Japan. Sponsor: Dr. Juan Saavedra, Laboratory of Clinical Science, NIMH, 10, Rm. 8D03.
6/18 Dr. Akio Sugino, Japan. Sponsor: Dr. John W. Porter, Laboratory of Genetics, NIEHS, Research Triangle Park, N.C.
6/19 Dr. Jean Grizard, France. Sponsor: Dr. Philip Gorden, Diabetes Branch, NIAID, 10, Rm. 8D243.
6/20 Dr. Ekaterini Ikonomou, Greece. Sponsor: Dr. Edward H. Oldfield, Neurosurgery Branch, NINCS, 10, Rm. 3E108.
6/20 Dr. John H. Willson, England. Sponsor: Dr. Roger O. Brady, Developmental and Metabolic Neurology Branch, NINCS, 10, Rm. 3D04.
6/21 Dr. Uri Liberman, Israel. Sponsor: Dr. G. D. Aurbach, Medical and Molecular Biology Branch, NINCS, 10, Rm. 3D20.
6/22 Dr. Masato Tanaka, Japan. Sponsor: Dr. George Khoury, Laboratory of Molecular Biology, NIB, 10, Rm. 400.
7/18 Dr. Mordechay Chevion, Israel. Sponsor: Dr. Gunther L. Eichhorn, Laboratory of Cellular and Molecular Biology, NIH, Bethesda.
7/24 Dr. Jeffrey B. Shiroky, Canada. Sponsor: Dr. Abner L. Notkins, Laboratory of Oral Medicine, NIDR, 10, Rm. 121.
8/22 Dr. Per Anders Dahlberg, Sweden. Sponsor: Dr. John L. Swanson, Rocky Mountain Laboratory, NIADDK, Hamilton, MT.
8/26 Dr. Bruce Weinstein, Clinical Endocrinology Branch, NIAID, 10, Rm. 8D13.
Marmoset Monkey Provides Model for Digestive Disease

Scientists and medical experts in the field of gastroenterology recently met at the Oak Ridge Associated Universities in Oak Ridge, Tenn., for a 3-day workshop to discuss the suitability of using the cotton-top tamarin for studying digestive tract disorders, particularly colitis and cancer of the colon.

The cotton-top tamarin is a species of marmoset monkey that is indigenous to parts of Central and South America. Its interest to scientists lies in its natural tendency to develop colitis (inflammation of the colon) and subsequent colon cancer. Cancer of the colon is one of the most commonly occurring cancers in humans, second only to lung cancer in men and breast cancer in women.

In most other animal models currently being studied for colitis and colon cancer, the diseases must be artificially induced in the laboratory. Thus, the marmoset may offer medical researchers new hope for understanding the developmental processes of these gastrointestinal disorders.

By tracking disease progress in the marmoset, scientists possibly can apply their findings to humans, which may provide new insights into the diagnosis, treatment and possible prevention of these diseases.

Dr. Kerl Vener, the colonic disease program director at the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases, helped organize the workshop.

According to Dr. Vener, "The workshop participants concluded that the marmoset deserves further laboratory study because it does appear to be a feasible model for studying the spontaneous onset of both colitis and colon cancer."

The workshop was sponsored by the ORAU's Marmoset Research Center, NAADDK, the National Cancer Institute, the Division of Research Grants, and the National Foundation for I.I.E.I. and Colitis.

Tooth Enamel Gene Found by DNA Technology

Using recombinant DNA technology, a team of dental scientists has identified, for the first time, one of the four genes responsible for the production of tooth enamel in humans.

This research could eventually lead to the "cloning" of natural fillings for decayed teeth—restorative materials with a structure and durability virtually identical to that of healthy teeth.

Dr. Malcolm Snead, a National Institute of Dental Research supported researcher, of the University of Southern California School of Dentistry, and associates at Houston's Baylor College of Medicine presented their findings at meetings of the International Association of Dental Research.

Progress in genetic engineering has proceeded at a faster pace than was anticipated. Four years ago, the production of human insulin and human growth hormone through recombinant DNA technology opened the door to the possibility of using this procedure to tailor-make virtually any protein.

These gene-splicing techniques are being applied not only in medicine, but in all fields of industry, and now in the field of restorative dentistry.

Tooth enamel is produced by a careful blend of four different proteins—three amelogenins and one enamelin—each manufactured by its own gene. In studies with mice, the investigators isolated the tissues that produce these proteins and extracted the messenger RNA (mRNA). As its name implies, messenger RNA relays instructions from the DNA—the gene's storehouse of genetic information that tells the gene what to do.

Drs. Snead, Harold Slavkin and colleagues used the newly isolated mRNA to prepare a gene identical to the largest amelogenin. They spliced this mouse gene into strains of common yeast, so that these living cell factories will begin to manufacture the enamel protein as programmed by the artificial genetic machinery. This method, it's hoped, will produce carbon copies of the mouse amelogenin protein.

The investigators have also applied these techniques to the studies of human enamel.

Using the mouse enamel protein and antibodies to learn more about its human counterpart, they found that one of the four enamel proteins in man is very similar in genetic sequence to that of the mouse. This is particularly significant because it demonstrates the usefulness of the mouse gene products in identifying and isolating human tooth enamel proteins.

A number of steps have yet to be accomplished before a new restorative material could become available. The other three proteins must first be isolated and cloned. The research team must then show that the four proteins will combine in the laboratory to form enamel with characteristics identical to the natural tooth.

Despite extensive work ahead, the investigators see exciting possibilities for practical application of their research. If the studies continue as planned, dentists in the future will be filling cavities with an enamel-cloned tooth enamel and adding the new material.
DES Quality Circles Working

Got a problem? Well maybe a Quality Circle can solve it. That's what's happening in the Division of Engineering Services. The director, DES, initiated a pilot Quality Circle program in June 1983. The program involves over 40 men and women in four circles: electric shop section, Shops Branch; power plant section, Maintenance Engineering Branch; shop stores section, Planning and Control Branch; and central clinic maintenance section, Maintenance Engineering Branch.

A quality circle is a small group of employees, generally from the same work area, who volunteer to meet regularly on agency time to identify, analyze, and solve work-related problems. The members receive training in problem-solving techniques and group dynamics.

Almost from the beginning, the DES circles have been identifying, analyzing, and solving problems. Each problem is presented to management for review and approval. The presentations generally are 90 minutes and consist of a discussion of the problem, the recommended solution, and a question and answer period. Here are some examples of major problems they tackled and the results.

The electric shop identified the need for cross-trade training, and recommended that a training position within DES be established to assist in identifying training needs and developing DES employees' skills. The director, DES, approved the recommendations and recommended the purchase of "state of the art" equipment that would maximize storage within part of the plant which was affecting turn time is approximately 3:30 p.m. For more information, call the R&W Activities Desk at 496-2461.

NICHD Director Addresses Women's Group On Estrogen Replacement Therapy

NICHD Director Dr. Mortimer B. Lipsett recently discussed the pros and cons of estrogen replacement therapy (ERT) with NICHD employees during a meeting sponsored by the Institute's Women's Organization.

Dr. Lipsett is an internationally known expert in endocrinology and has published more than 260 scientific papers on that subject. During the discussion, Dr. Lipsett talked about some of the studies that made estrogen replacement therapy (ERT) controversial. "The clear advantages of ERT are the lessened or eliminated menopausal symptoms that women experience when their own production of estrogen has stopped or diminished following natural or surgical menopause," Dr. Lipsett said.

These symptoms may include hot flashes and painful intercourse because of vaginal dryness. Twenty percent of all menopausal women have symptoms severe enough to seek medical attention. Another benefit of ERT is its role in the prevention of osteoporosis, a debilitating, chronic disease that affects some 20 million Americans, especially older women, Dr. Lipsett said. It has been estimated that about 1.3 million fractures attributable to osteoporosis occur every year in people 55 years of age and older. "The use of estrogen after menopause has been shown to decrease the rate of calcium loss from bone and possibly to decrease the occurrence of heart attacks as well," Dr. Lipsett said.

However, some studies indicate that estrogens are associated with an increased risk of endometrial cancer and possibly breast cancer, and produce such side effects as swollen breasts, nausea, vaginal discharge, headache, fluid retention and weight gain. Early findings of new research indicate, however, that progestins, taken in the proper dose and at 2-3 month intervals, will offset the carcinogenic risks of ERT.

During a recent Consensus Development Conference on Osteoporosis, a panel of experts concluded that the benefits of estrogen replacement therapy outweighed its risks, and suggested increased calcium intake and weight-bearing exercise to further reduce the risks of osteoporosis.

Dr. Lipsett believes that chronic fibrocystic disease (lumpy breasts) and a family history of breast cancer are contraindications for ERT. He recommended that each woman with serious postmenopausal symptoms—in consultation with her physician—carefully weigh her individual needs and risk factors before starting estrogen replacement therapy.

Pancreatic Cancer: Hard to Diagnose and Usually Fatal

Pancreatic cancer is a "silent" disease, without symptoms, until it is advanced. Very little is known about what causes it or how to prevent it.

An organ about 6 inches long located behind the stomach, the pancreas has two functions: it sends insulin into the bloodstream to control the amount of sugar in the blood, and sends pancreatic juice into the intestine to help digest food.

Small tubes or ducts in the organ transport the pancreatic juice and—if cancer occurs—it is usually in these duct cells.

From 1951 to 1978, the death rates for pancreatic cancer in the United States rose almost 30 percent to about 11 deaths per 100,000 men and about 7 per 100,000 women.

The incidence of pancreatic cancer among U.S. blacks is about 1.5 times higher than for whites. Hawaiians and American Indians are also at a high risk.

Seventh-Day Adventists and Mormons have a lower than average death rate, and Jewish men have a higher than average death rate. Worldwide, the United States and Northern European countries, including Great Britain, have high incidences of pancreatic cancer and Polynesians have a very high rate.

The disease is usually fatal; only 4 percent of patients live more than 3 years after diagnosis. The very few patients whose cancers occur in the insulin-producing cells—not the duct cells—tend to live longer, about 30 percent of these patients live more than 3 years after diagnosis.

After 30, this cancer increases in both men and women in every population studied. An excess risk has been established among cigarette smokers, although the magnitude of the risk is not so great as with lung cancer.

Diabetes mellitus has been linked in some studies with pancreatic cancer, but it is not known if cancer causes diabetes-like changes, or if diabetes makes individuals prone to cancer. No clear association has been found between diet and pancreatic cancer.

Research has focused on ways to diagnose pancreatic cancer before it is advanced enough to cause symptoms. Ultrasound and CAT scans are being tried, but to date only a biopsy yields a certain diagnosis.

Surgery, radiation therapy, and anticancer drugs are used to treat pancreatic cancer, but so far have had little influence on outcome.

In 1975, the National Cancer Institute established the National Pancreatic Cancer Project to stimulate research on the causes, diagnosis, and treatment of the disease.

For more information, call 1-800-4CANCER.
Dr. Price, NIGMS, Retires; Served NIH 38 Years

Dr. Vincent E. Price, deputy director of the National Institute of General Medical Sciences' Cellular and Molecular Basis of Disease Program and special assistant to the Director, NIGMS, recently retired after 38 years of service in the NIH community.

Describing him, Dr. Ruth L. Kirschstein, Institute Director, said, "He is the kindest, most generous person I have ever known ... a virtual institution at NIGMS." Both she and Dr. Leo H. von Euler, NIGMS deputy director, referred to Dr. Price's retirement after 22 years with the Institute as "the end of an era."

Immediately after graduating from medical school, Dr. Price began his NIH career. He worked in the Laboratory of Biochemistry of the National Cancer Institute from 1946 to 1960. During that time, he progressed from staff scientist to assistant chief and then to acting chief of the laboratory.

He also served as a visiting scientist at the Institute of Cytophysiology in Copenhagen, Denmark, for 1 year. Dr. Price then joined the Division of General Medical Sciences, the predecessor of NIGMS, as program administrator for the Medical Student Research Training (MSRT) Program. The purpose of this program was to provide medical students in basic research by making research training available during summers and other periods when they were not attending classes.

After NIGMS was created in 1962, Dr. Price was instrumental in expanding and changing the MSRT Program into what is now called the Medical Scientist Training Program (MSTP). The MSTP is larger in scale and supports student training on a full-time basis leading to the combined M.D.-Ph.D. degree. Since its inception, approximately 2,000 individuals have received training through the program.

Dr. Price has found this aspect of his position to be the most rewarding and challenging. He enjoys "helping young people along in their careers" and "trying to break through the barriers between basic research and clinical medicine."

His avid interest in research training led to his appointment as chairman of a task force on the development of a 10-year plan for NIH training programs from 1967 to 1976.

In addition, he also served as NIH project officer for a National Academy of Sciences/National Research Council study of national needs for biomedical and behavioral research personnel, conducted from 1974 to 1976.

Another major contribution Dr. Price made to the evolution of NIGMS was his "recognition that cellular and molecular biology were research areas which should be studied through the support of research grants," according to Dr. Kirschstein.

The identification of such a need led to the creation of the Institute's Cellular and Molecular Basis of Disease Program, which currently has a budget of approximately $126 million.

Dr. Price received a B.A. from Oberlin College and an M.D. from the University of Michigan. He is a PHS commissioned officer and a member of the American Society of Biological Chemists, American Association for the Advancement of Science and the Association of American Medical Colleges.

During his retirement, Dr. Price plans to keep abreast of the rapid advances in research being reported in scientific literature and will continue to follow with great interest the careers and achievements of the MSTP graduates. He also hopes to become more active in community affairs.

He is married and has four children, who share his love for science and mathematics. Their careers range from veterinary medicine to nuclear fusion, molecular genetics, and business administration/accounting.

Dr. Miller, NIGMS, Recognized by Biological Chemists Society

Dr. Charles A. Miller, director, Cellular and Molecular Basis of Disease Program of the National Institute of General Medical Sciences, was recently elected as one of the first two Distinguished Service Associates by the American Society of Biological Chemists.

This new and prestigious classification of membership will be awarded only on rare occasions to honor persons who have made outstanding contributions to the discipline of biochemistry as well as providing assistance to individual biochemists.

Keppie Engel, formerly with the then National Institute of Arthritis and Metabolic Diseases and presently with the National Science Foundation, was the other honoree. These special awards acknowledge the importance of the NIH and NSF extramural grants programs and the dedication of their scientific personnel.

Since joining NIGMS in 1961, Dr. Miller has developed and guided major research and training programs in several basic biomedical science disciplines. The American Society of Biological Chemists represents a large body of scientists whose research, much of it supported by the NIH, has fostered many of the major advances in the biomedical sciences in recent years.

The value of life lies not in length of days, but in the use we make of them.—Montaigne
Walter Chakwin Retires

Walter "Walt" Chakwin, chief, Supply Operations Branch, Division of Administrative Services, retired on June 1, from a government career of 48 years; 23 years were with NIH.

Mr. Chakwin had served in this position since 1972. The Supply Operations Branch manages the supply operations program which includes central stores, inventory management, shipping, and receiving. He will also act as grants management officer, chief of the Extramural Services Branch of the National Eye Institute.

Before joining NIH, Mr. Chakwin retired from the D.C. Fire Department. He was previously employed by the Bureau of Internal Revenue and the Interstate Commerce Commission.

He joined NIH in 1962 as a clerk-typist in the central stores sub-unit, property and supply section. Supply Management Branch. During his tenure at NIH, Mr. Chakwin served as president of the NIH Recreation and Welfare Association.

His coworkers and friends wished him "Good Luck" at a retirement luncheon held in his honor with more than 200 family and friends in attendance.

Geoffrey Grant Appointed NEI Extramural Services Branch Chief

Geoffrey E. Grant has been appointed chief of the Extramural Services Branch of the National Eye Institute. In his new position, he will provide overall fiscal and administrative management for NEI's extramural program, including all research grants and fellowships, small grants and pilot projects, and research contracts. He will also serve as grants management officer, directing staff in the receipt, administrative review and award of research grants.

Mr. Grant replaces Anna Marie Perrell who retired on May 31.

Mr. Grant comes to NEI from the NIH grants policy office where he held the position of grants management specialist in the office of extramural research and training, OD. During his tenure there, he received an NIA Special Achievement Award in 1982 for coordinating a group of grants management specialists who reviewed the business management of the Teaching Nursing Home Awards Program.

A graduate of St. Michael's College in Vermont in 1968, Mr. Grant earned his M.Ed. in higher education administration from the University of Vermont in 1970. He entered the U.S. Air Force as a curriculum evaluator and later worked in Air Force research and development contracting at Randolph Air Force Base in Texas.

Mr. Grant is currently a member of the Board of Directors of the NIH Federal Credit Union and a member of the NIH administrative training committee, which is responsible for the NIH management intern program.

Anna Marie Perrell Retires After 37 Years at NIH

Anna Marie Perrell, grants management officer for the National Eye Institute since its inception and chief of the NEI's Extramural Services Branch, retired on May 31. Her retirement capped a 37-year career in the Public Health Service, all of it at the National Institutes of Health.

When she began her career at the NIH as a clerk-typist in the Division of Research Grants, that newly-established division was located on the 114 corridor of Bldg. 1.

Ms. Perrell believes she is the last of those original DRG staffers remaining at NIH. Over the years, she served in other positions in DRG and in the Division of Environmental Health Sciences when it became a part of NIH.

Ms. Perrell came to NEI in 1970. As grants management officer, she was responsible for the business management of the Institute's research grants program. She was involved in planning, organizing, directing, and promoting this program. She also directed the Extramural Services Branch staff in providing grants management assistance to the NIH extramural community and to the vision research community.

Well-recognized as an authority in the grants management field, Ms. Perrell has served on several NIH-wide panels, among them the Administrative Training Committee, the Women's Advisory Committee, STEP, and the Grants Management Advisory Committee of which she considers herself "a lifelong member."

In summarizing her accomplishments, Dr. Ronald G. Geller, associate director for Extramural and Collaborative Programs, said, "Anna Marie Perrell made a commitment to the mission of the Public Health Service which is exceeded by few and sets a high standard for us all."

During her career at NEI, she presented grants management seminars to scientists at vision research centers. Then in 1983 she began and innovative series of seminars for administrators at grantee institutions.

Leaving her management career at NIH, she will move into yet another career at her church. She is chairman-elect of the church board and chairman of this year's fall bazaar, for which she is directing 20 volunteer handycrafters and lining up a staff of 75 workers.

Ms. Perrell and her husband share an interest in travel and gardening. During this summer they will travel to the southwestern states visiting forts and historic museums.

When they are at home, she will raise late-blooming gladiolas that she hopes will be prize winners at the Montgomery County Fair. Many of their zinnias, tea roses, and marigolds have won ribbons in the past 25 years.

Biosafety Level Guidelines Published by CDC and NIH

The Division of Safety, OD/ORS has announced the availability of "Biosafety in Microbiological and Biomedical Laboratories," a set of guidelines.

A collaborative effort by the Centers for Disease Control and the National Institutes of Health, "Biosafety in Microbiological and Biomedical Laboratories" describes combinations of standard and special microbiological practices, safety equipment, and facilities that constitute biosafety levels 1-4.

Similar in concept to the P1-P4 levels described in "NIH Guidelines for Research involving Recombinant DNA Molecules", biosafety levels 1-4 are recommended levels for working with a variety of infectious agents in the laboratory setting.

The biosafety levels described are advisory and are intended to provide a voluntary guide and code of practice on laboratory hazards and precautions associated with the handling of specific pathogens.

These guidelines emphasize an active process for assessing risk rather than summarily placing agents in rigid categories. The agent summary statements review well-documented hazards associated with specific agents and provide guidance for the selection of appropriate precautions.

The underlying principle is that no single set of specifications is applicable in all situations involving an infectious agent. In summary, "Biosafety in Microbiological and Biomedical Laboratories" underscores the importance of thoughtful project planning and management in assessing the potential risks associated with individual exposure.

Multiple copies may be obtained by calling GPO at (202) 783-3238. Refer to GPO Stock Number 017-023-00167-1. The cost is $4.00 per copy. For single copies, call your BID Safety and Health Consultant, Occupational Safety and Health Branch, DS, at 496-2346.

Computer Symposium Slated

Come to the Computer Symposium Aug. 1 and 2 to learn the latest in computer technology.

The symposium is being held at Wilson Hall, Bldg. 1, from 8:30 a.m.-5 p.m. and is sponsored by Entre' Computers.

If you are interested or have any questions, call the R&W Activities Desk at 496-6061.
**New Medical Neurology Branch Created by NINCDS**

NINCDS has established a new Medical Neurology Branch to conduct clinical and related basic research on the epilepsies, motor control, neuropharmacology, and neuronal excitability.

Dr. Roger J. Porter, a NINCDS neurologist, has been named chief of the new intramural branch, which contains four research sections.

Prior to assuming his new duties, Dr. Porter was chief of the extramural Epilepsy Branch, NINCDS, where he oversaw the antiepileptic drug development program and administered NINCDS grant and contract portfolios on convulsive disorders. Dr. B. G. White will manage these extramural activities until a permanent replacement can be found.

Dr. Porter also previously directed a clinical epilepsy section in the Experimental Therapeutics Branch, which is another division in the Institute's intramural program. This section has been transferred to the new branch, where Dr. Porter will continue to manage and conduct investigations on the diagnosis and treatment of the epilepsies.

Another part of the new branch, the Human Motor Control Section, will be directed by Dr. Mark Hallett, who joined NINCDS in April as the intramural program clinical director. Researchers in this section will use electrophysiology and electromyography to study the control of movement in normal volunteers and in people with motor disorders such as Parkinson's disease, cerebellar ataxia and spasticity.

Dr. Ronald D. Polinsky has been selected to direct the new branch's Clinical Neuropharmacology Section, which will conduct research on the role of human neurotransmitters in degenerative disorders and aging. Special emphasis will be given to the study of the autonomic nervous system and to genetic aspects of Alzheimer's disease.

The Neuronal Excitability Section will be the center for basic research in the new branch. This section will evaluate the role of neurotransmitters and effects of antiepileptic drugs on normal and abnormal nerve discharges in mammalian nerve tissue. A chief for the section has not yet been named.

The creation of the Medical Neurology Branch brings the total number of NINCDS intramural Research Program components to 8 clinical research branches and 11 basic science laboratories.

**FAES Grad School Announces Schedule for Fall**

The FAES Graduate School at NIH has announced the schedule of courses for the Fall Semester, which will begin Sept. 17 on the NIH and USUHS campuses.

Registration will be held Sept. 5-11. Tuition is $40 per credit hour and courses may be taken for credit or audit.

Fall schedules are available in the Graduate School office in the Clinical Center, Rm. 2-C-207A and in the Foundation Bookstore Rm. B1-L-101. To have one sent, call 496-7977.

**Dr. Friedman Receives New Appointment in DRG**

Dr. Mischa E. Friedman was recently appointed chief of the Referral and Review Branch, Division of Research Grants.

Dr. Friedman will direct all activities concerning the referral of grant applications requesting support from the Public Health Service. He will also direct initial scientific review of grants applications submitted to NIH. In this capacity, he will be responsible for the overall management of approximately 90 DRG review groups.

Dr. Friedman, a native of Worcester, Mass., received his B.S. degree in bacteriology from the University of Massachusetts. He then attended the University of Illinois where he received his M.S. in 1948 and Ph.D. in 1953.

Since 1976, he had served as assistant chief for clinical sciences review in the RR branch. He was responsible for assuring the adequacy of peer review activities for 18 of DRG's study sections. Also, he provided advice to the branch chief concerning the functions of study sections and the need for new review groups and areas. He served on the NIH grants associates board and on NIH/DRG committees regarding grant application review policies and training of extramural program staff.

From 1970 to 1976, he was executive secretary of the allergy and immunology study section, DRG, responsible for the initial administration and scientific review of research grants. Research Career Development Award and NRSA Individual Postdoctoral Fellowship, and institutional training grant applications.

**NIGMS Grantees Win Awards**

Four researchers, all grantees of the National Institute of General Medical Sciences working in three very different fields, have recently won prestigious awards.

Dr. Henry Taube, winner of the 1983 Nobel Prize in Chemistry, will be the 1986 recipient of the Priestley Medal, the highest honor given by the American Chemical Society. The award, latest in a long list of Dr. Taube's honors, will be presented at the society's spring 1986 meeting.

Dr. Taube, professor of chemistry at Stanford University, has made many important contributions to the development of modern inorganic chemistry. He is probably best known for his research on oxidation-reduction reactions as related to the action of enzymes, the molecules that catalyze many different life processes.

The first G. Whitaker International Burns Prize has been awarded to Dr. Charles Baxter, professor of surgery at the University of Texas Health Science Center at Dallas and Director of the University of Texas Parkland Burn Center. This $10,000 award was established to recognize "outstanding contributions of experts from all countries in the field of burn pathology."

Dr. Baxter has contributed significantly to the development of improved treatment for burn patients, especially in the areas of fluid replacement, nutritional management, and skin grafting.

Allan C. Spradling of the Carnegie Institution of Washington and Gerald M. Rubin of the University of California, Berkeley, have won the 1982-83 Newcomb Cleveland Prize from the American Association for the Advancement of Science (AAAS) for two original articles in the Oct. 22, 1982 issue of Science. These articles described a new method for transferring genes into the germ (reproductive cell) line of Drosophila melanogaster (the "fruit fly" commonly used in genetic research), a technique the authors developed.

The AAAS selection committee cited the new method as "a technical achievement of far-reaching consequence."

**Symposium on Gonadotropins To Honor Noted Endocrinologist**

Dr. Griff T. Ross, a noted endocrinologist who spent 20 years at NIH, will be honored at a symposium to be held on gonadotropins, the brain hormones that regulate reproductive processes.

The symposium, to be chaired by Dr. Mortimer B. Lipsett, Director, NICHD, will take place on Aug. 10 in Bldg. 31 C, Conf. Rm. 10, from 9 a.m. to 5 p.m.

The program will include 20 speakers, all of whom worked with Dr. Ross. Short presentations will be given on the history, use, measurement, biochemistry, and molecular biology of gonadotropins. Dr. Ross's contributions to the field of endocrinology include advances in determining the hormonal regulation of ovarian function. While at NIH, he served as chief director for NICHD, deputy director of the Clinical Center, and deputy associate director for Clinical Care.
Histotechnicians Retire, Pathology Section Closes at NCI After 47 Years

Some 125 years of working talent and skill retired on June 29 in the persons of four staff members of the Pathology Technological Section of NCI's Laboratory of Pathology, which section, after 47 years of existence, will close.

Retiring were: section chief Barbara Coolidge, 30 years; Clara Mauck, 35 years; Ruby Thompson, 32 years and Lindell Dove, 28 years.

With their departure, their former tasks will be contracted out.

Though too modest to sing their own praises, their colleagues and coworkers responded with superlatives on their technical expertise, led by Dr. Lance Liotta, chief of the Laboratory of Pathology.

He said, in part:

"Anybody can follow work directions but it takes combined instinct and judgment to know just how to hold the slide, how much specimen to put on it, how warm to keep it, precisely where to slice, and many other variables."

"It was such intangibles that made them experts," he said.

Their skills were so important, he indicated, because "animal tissue histology (microscopic study of cells) is the end point of many experiments."

Dr. Harold L. Stewart, the 84-year-old scientist-emeritus who started the pathological technology laboratory 47 years ago and now works in the NCI registry of experimental cancer, said, at the four's farewell party:

"I feel just like a country doctor. I presided at the birth of the organization, saw it through childhood problems, and now am witnessing its death. But the judgment, precision, and dedication of these four have contributed significantly to our current registry of experimental cancer, which is the largest such registry in the world."

Mrs. Coolidge is coauthor of the manual, "Animal Histology Procedures," which has gone through two editions and is the standard "cookbook" for histologists. In step-by-step precision, it clearly explains each type of laboratory procedure.

Dr. Liotta says, "It's a must for any histology worker, from the new technician to the experienced pathologist." Coauthor Ruby Howard, now supervisor of the histopathology section of the Laboratory of Pathology, says that the entire group contributed to the procedures, but Mrs. Thompson was the one who typed the copy for both editions.

Developed Sectioning Technique

Dr. Richard Knazek, now on sabbatical in Switzerland from the NCI Laboratory of Pathophysiology, recalls how the group invented a new sectioning technique for the capillary system that his laboratory group had developed.

Because the tumor cells were bathed in nutrients passing from the hundreds of capillaries surrounding the cells, they grew in clumps instead of the usual single layers that
grow in a petri dish.

Dr. Knazek says, "Those technicians had to devise a way to remove these bundles from the cylinder without crushing the cell cultures, replace the fluids with paraffin, and embed them on end so that they could section across the capillary tubes."

"Then they had to slice through the tough capillary fibers without crushing them or distorting the homology of the cell masses growing around the capillaries. I don't know how they did it, but in a few weeks we got lovely cross-sections of our cultures with everything intact. Their perseverance contributed greatly to the success of the method and its introduction to other labs throughout the United States."

The animal tumor registry now contains 659,252 accessions or sets of tissue blocks, but since one accession could represent from one to 40 blocks from just one animal, the inventory is many times larger. Too, many of the specimens had to be re-embedded from crumbling paraffin blocks, some dating from 1937.

Trained Histotechnicians

The four technicians also did substantial one-on-one training in their lab.

Dr. Michael Orlando, now director of the histology laboratory of Faulkner Hospital in Warrenton, Va., did his residency at NCI in the Laboratory of Pathology. "They trained me," he says, "but in a way they spoiled me. They set a standard of excellence I have never been able to get from my own staff without constant insistence. When I hired a new histotechnician, I sent her straight to NCI for training so she would get started correctly."

Dr. John Hershberger, director of the Smithsonian Registry of Tumors in Lower Animals, learned of the quality work done by the animal histology group in 1967 when he was developing the Smithsonian tumor registry.

"They were basic to the startup of the registry and they played a role right up to the end," says Dr. Hershberger. "When I got a new technician, I wanted her trained right, so I sent her to work with the experts at NCI."

Another group they helped was in the National Marine Fisheries Service of the National Oceanic and Atmospheric Administration (NOAA). In 1973 when the Oxford, Md., laboratory expanded its tumor work, the histotechnicians needed to learn how to use some of the more sophisticated equipment and to master some particular procedures on serial sectioning and special staining.—Joyce Doherty.

A Fantastic Benefit

R&W, in conjunction with radio station WPGC, is sponsoring a NIH Day at Wild World Aug. 11.

Funds raised from the event will benefit Camp Fantastic.

For more information, call the R&W Activities Desk at 496-6061.

Don't "Cheat" Yourself

Come and join the R&W on a trip down the Cheat River in West Virginia on Aug. 11.

The trip will last all day and participants will be traveling down the river on Duckies, which are one-man rafts.

Cost is $49; participants must provide their own transportation to the river. For more information, call the R&W Activities Desk at 496-6061.
Promising Environmental Health Research Reported by NEIHS Task Force on Planning

Areas holding the greatest promise for research advances in environmental health sciences through the end of the decade— including biological mechanisms and toxic agents—have been reported by the Third Task Force on Research Planning in the Environmental Health Sciences.

Eleven subtask force panels with various areas of scientific emphasis presented their recommendations for research in June at the end of a week-long series of working sessions held at the National Institute of Environmental Health Sciences in Research Triangle Park, N.C.

The goal of the Third Task Force was to identify particular scientific opportunities in areas where increased knowledge would improve our ability to deal with the types of environmental health problems expected through 1990. The reports represent combined efforts of the more than 85 participants in the Task Force extending over many months.

The conclusions and recommendations reflect collective judgments reached by consensus among the participants, based on their expertise as individuals and on their joint review of background documents summarizing current knowledge and research needs in the various subject areas considered.

As requested by Congress, the reports concentrate primarily on those areas of research promise in which scientific advances can be expected to have the greatest impact in preventing or alleviating environmental health problems.

The five broad topic areas addressed in these reports were the following: 1) the biological mechanisms through which physical and chemical agents give rise to disease, 2) methods for assessing the health significance of exposure to toxic agents, 3) research strategies for preventing environmentally provoked disease, 4) the organization and structure of environmental health research in the U.S., and 5) information exchange in the environmental health sciences.

Among major recommendations for advancing research issues relevant to environmental health research were:

- Exploit developments in cellular and molecular biology as quickly as possible in research on the mechanisms of environmentally provoked disease.
- Such research will require a pool of appropriately trained scientists, dedicated to the problems of discovering and understanding the actions of environmental pollutants on cells. Training programs are needed especially for persons with clinical backgrounds to enable them to obtain an understanding of, and become proficient in, the use of current and developing concepts and methods of molecular and cell biology.
- Evaluate in vivo (lab) and whole-animal tests, using information about basic mechanisms of reproductive processes and toxicity; exploit these tests to identify agents that result in infertility or birth defects.
- Expand the data base on the interaction of chemicals with the immune and host defense systems, to allow more appropriate decision making on chemical usage and risk, and to provide the foundation for understanding structure-activity relationships and mechanisms of chemically induced injury.
- Continue clinical studies to determine whether chronic low-level exposure to toxic substances constitute a hazard that contributed to immunologic dysregulation, autoimmune disease, and cancer.
- Foster application of new immunologic methods (monoclonal antibodies) for quantitative detection of environmental contamination and adverse effects of xenobiotics (drugs);
- Increase research on the molecular sites at which mutagens may act, to determine whether there are specific hot spots that are particularly sensitive to mutagens;
- Establish liver tissue banks, to include specimens from normal as well as abnormal individuals.
- Dr. Thomas E. Malone, NIH Deputy Director, one of the invited speakers at the June meeting, said, "I think that in the decades ahead the problems of pollution, of environmental control, of population control and nutrition requirements perhaps will present the most severe challenge to science. When one looks at the challenges in environmental health and one looks at ethical and social problems, Task Force III takes on the obviously greatest significance.

At NIH we view this as an extremely important activity not only because it was congressionally mandated, but because earlier research is so vast and so broad that we obviously have to focus our attention and resources and intellectual energy on the most promising research needs in this most important area."

The Task Force, divided into 11 panels with various areas of scientific emphasis, is co-chaired by Dr. Bernard Goldstein, assistant administrator for Research and Development, U.S. Environmental Protection Agency, and Dr. Arthur C. Upton, chairman, Institute of Environmental Medicine, New York University Medical Center, and former Director of the National Cancer Institute.

Dr. David P. Rall, Director of NEIHS and the National Toxicology Program, said, "The Task Force will help those in the field identify particular scientific opportunities in areas where increased knowledge will improve our ability to deal with the types of environmental health problems anticipated through the end of the decade."

NIA Scientist Receives Prestigious French Award

Dr. Stanley I. Rapoport, chief of the National Institute on Aging's Laboratory of Neurosciences, recently received a Silver Medal from the City of Paris. The mayor of Paris presented the award for research conducted under Dr. Rapoport's direction, involving positron emission tomography and the measurement of cerebral metabolic rate of glucose.

Dr. Rapoport and his colleagues in the Laboratory of Neurosciences demonstrated that resting cerebral metabolic rate of glucose does not decline with age in subjects who are extremely healthy. Glucose metabolism provides a direct measure of brain activity.

These conclusions are based on research on 40 healthy men between the ages of 21 and 83 years, and differ from conclusions from some other studies with positron emission tomography.

According to Dr. Rapoport, this is due in large part to the fact that subjects are carefully screened for such diseases as atherosclerosis, diabetes, and organic brain syndrome which increase in age and might contribute to altered brain function.

Thus it appears that, despite many morphological and neurochemical changes which have been demonstrated in the aged human brain, compensatory processes of plasticity and inherent redundancy of neuronal networks are sufficient to maintain brain function at a normal level in the elderly.

Furthermore, Dr. Rapoport and his colleagues have established critical baseline data for metabolic studies with positron emission tomography which now make it possible to examine, by comparison, subtle effects of disease on brain metabolism and function.

In other studies using positron emission tomography, the Laboratory of Neurosciences has demonstrated the metabolic rate for glucose is elevated by 30 to 40 percent in young adults with Down syndrome, and that subtle decrements in metabolic function in Alzheimer's disease are correlated with specific neuropsychological deficits.
FORSKOLIN
(Continued from Page 1)

cyclase in a direct manner, unlike other known stimulators of the enzyme's action.

In addition, forskolin was found to markedly potentiate effects of hormones on the enzyme. These actions of forskolin make it a unique and powerful tool for the investigation of both the enzyme adenylate cyclase and the role of cyclic AMP in physiological processes.

This basic research allowed Dr. Daly and his colleagues to predict possible therapeutic actions of forskolin. Since their original publication in 1981, many of their predictions have been verified by other laboratories as well as their own.

Using human platelets (blood cells involved in the clotting process), Dr. Daly and collaborators, Drs. A.M. Siegel and J.B. Smith, examined the physiological and biochemical responses of a single cell type (the platelet) to forskolin.

The investigators found that forskolin can interrupt the clotting process by inhibiting the clumping of platelets. This inhibition appears to be the result of forskolin's action on the cyclic AMP system of the platelet, indicating a potential therapeutic value as an anti-clotting agent.

Glaucoma, an eye disease afflicting 2 million Americans over 35, is characterized by excessive fluid pressure inside the eye that can lead to blindness. Yale University investigators have used forskolin to reduce fluid pressure in the eyes of rabbits, monkeys, and human volunteers.

Forskolin works in the eye in much the same way it does in platelets. It stimulates the enzyme adenylate cyclase, which increases cyclic AMP in the eye causing a reduction in the flow of fluid into the eye and thus lowers intraocular pressure.

Because the drug's action is understood, the Yale investigators said it "would lead us closer to an understanding of what actually regulates eye pressure and in that way we might get clues as to what causes certain types of glaucoma. We don't know yet whether this is an important therapy. We think it has a chance of being an important one."

This understanding of forskolin's action is contributing to its popularity as both a research tool and potential therapeutic agent. Although different hormones affect different cellular responses, many work in a similar manner, that is, the adenylate cyclase-cyclicAMP route.

Other examples of forskolin research include:
• Forskolin as initially found by Dr. N. DeSouza and colleagues in Bombay, India, has potential as a hypotensive agent and is a replacement for digitalis in cardiac insufficiency. It is currently being used in Germany in clinical trials.
• In fat cells, forskolin triggers the mobilization and breakdown of fat deposits and amplifies the effects of hormones normally involved in control of fat metabolism.
• It has been used to correct excessive urine production in rats with hereditary diabetes insipidus (a metabolic disorder resulting in a deficient quantity of antidiuretic hormone causing increased urine production, great thirst, and a voracious appetite). Forskolin in this case corrects for the absence of the hormone vasopressin, which is responsible for increasing water permeability of the kidney.
• In studies with frogs, forskolin stimulated adenylate cyclase activity in injured nerve tissue, suggesting its use in regenerative nerve growth following trauma.
• Researchers at Emory University have used forskolin as a tool for studying gastric secretions, providing evidence that these actions are mediated by the activation of adenylate cyclase.
• Cyclic AMP has a direct effect on rapidly growing cells. Forskolin is now being used in cancer cell studies.
• Forskolin alone seems to be a remarkable substance. Drs. Daly and Seamon, in addition to their pioneering work on forskolin's mechanism of action, have also developed a radioligand binding assay for forskolin. This assay is useful in testing for other drugs that may mimic, augment, or prevent the action of forskolin.

As for the future, forskolin studies continue to explode across the research journals. Dr. Daly looks forward to the total synthesis of the molecule (only part has been synthesized to date), to structural modifications to the molecule, and perhaps to the discovery of a naturally occurring forskolin in these varied tissues.

Coleus forskohlii, a particular species of the Coleus plant, is still used in Indian folk medicine today.