

The NIH Record

A 'Renaissance Lady'

McFarland's Chemistry Extends from Molecules to Man

By Francis X. Mahaney, Jr.

Vivian McFarland smiles demurely, looking out her office window at the autumn trees ablaze with color. During her 31 years as a chemist for NCI, McFarland has never failed to take notice of the changing seasons, or the uniqueness of our lives.

"Life still holds the same fascination and beauty" as it did more than three decades ago when she stepped off a bus at the dingy Trailways bus station in Washington to begin her career at NIH, she says.

There was no beltway back then, she recalls. Most people still lived in the city. And for many District residents, the trip to NIH meant a 20-cent streetcar ride to the outskirts of the city, where a D.C. Transit bus would travel from Friendship Heights or Silver Spring to NIH.

The bumpy ride in the streetcar on a winter day with the snow falling, and the sounds of its clanking bell urging motorists off the tracks, were unforgettable.

Just as unforgettable in her memory are all the people she has met and helped along the way. It may be an elderly man in need of food, or someone who needs to be comforted. Whatever the reason, McFarland is always there to help.

Recently, McFarland was awarded an EEO special achievement award. To her fellow laboratory workers, the award came as no surprise. She is constantly helping the "disadvantaged and the poor, and advocating the hiring of minorities and the handicapped," her coworkers say.

At St. Stephen and the Incarnation Episcopal Church in Northwest Washington, she has been active for many years in programs to feed the poor and the elderly.

She is a key participant in a District ex-offenders task force, helping ex-felons return to society and their families. Recently, her work on the task force has broadened to include teenage offenders now living in halfway houses. "Maybe with enough care, perhaps I can help turn their lives around," she says. McFarland is also treasurer on the board of the Washington Free Clinic.

"Life is full of injustice, sorrow and hurt," she says. "But if I can be there to help someone in even a small way, I may be able to make a difference."

For the past 30 years at NIH, McFarland has been a strong advocate of employment opportunities for minorities and the

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NIAID: Flourishing at Fortieth Anniversary

Shortly before the turn of this century, boatloads of immigrants began heading toward America's open arms. Along with their many dreams, energies and talents, some immigrants unknowingly and unfortunately carried deadly infectious diseases such as cholera and yellow fever, which at that time were pandemic around the world.

To prevent these diseases coming onto America's shores, a screening program was established at Staten Island's U.S. Marine Hospital at the port of New York. An important part of this program was the founding in 1887 by Dr. Joseph J. Kinyoun of the progenitor of the National Institute of Allergy and Infectious Diseases, called the Laboratory of Hygiene (later renamed the Hygienic Laboratory). Kinyoun's purpose was to bring research, particularly the new science of bacteriology, into the fight against disease.

Up until this time, the only means of controlling epidemics had been through quarantine; it was not known what actually caused these diseases imported from other countries. But with new microscope techniques learned by Kinyoun in Europe, U.S.



NIAID's 40th anniversary celebrates the creation in 1948 of its precursor institute. Before even that, however, research on Rocky Mountain spotted fever began in Montana, as this 1916 picture featuring Dr. R.R. Parker and his wife shows.

scientists for the first time could detect disease-causing organisms. Physicians no longer had to rely solely on clinical signs to determine whether a person might be carrying a disease. (See **ANNIVERSARY**, Page 6)

Another 'Pearl Harbor'

AIDS Challenge Offers Chance to Improve Society

Viewed through a lens tempered by reason and compassion, the AIDS epidemic in the United States could become the occasion of new social, educational and health policies that could improve the country.

This optimistic news came from Admiral James D. Watkins (Ret.), chairman of the Presidential Commission on the HIV Epidemic, who spoke to a packed Lipsett Auditorium on Nov. 30, the eve of the first World AIDS Day sponsored by the World Health Organization.

"This virus could be a Pearl Harbor to spur us into action if we allow it to be," said Watkins, a former chief of naval operations and the leader who helped guide the president's commission off the "rocks and shoals" of inaction that impeded the first quarter of its year-long inquiry.

The commission delivered its widely praised report, on time, to President Reagan on June 27.

Describing the scope of his commission's duties as unprecedentedly broad in comparison with other presidential commissions, Watkins attributed success to two factors: a refusal to preach morals to the American public and a willingness to listen to the advice of the "best and brightest" authorities.

"We conducted 43 hearings and discovered that 85 percent of what they were telling us was consensus," he said. "We knew right then we had a winner of a report."

The cornerstone of the commission's nearly 600 recommendations is that persons with AIDS should not have to deal with discrimination in the workplace, housing market, legal system, health care delivery system or insurance world, in addition to struggling with HIV infection.

Antidiscrimination laws should extend to both public and private sectors and should include not only those already sick with AIDS but also those diagnosed with HIV infection, Watkins said. In effect, AIDS should not require any special legislation of its own but rather be lumped in with laws that already protect the victims of any other disability or handicap that might impair a citizen, regardless of cause.

Confidentiality laws, too, require amendment so that public health officials can get a clearer picture of how far HIV has penetrated society. Watkin's commission has drawn up eight exceptions to current laws, the effect of which would balance patients' privacy with the public's need to know.

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Watkins Says Crisis May Be Good Opportunity

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"This will allow us to get the data we so desperately need, especially considering the 7-year latency period of HIV and such worrisome cofactors as drug use and sexual activity among the young. We have to go overboard at this time to stem the tide of potential infection."

Referring briefly to the moral controversy surrounding the acquisition of many AIDS cases, Watkins dismissed such qualms as "dust in the air" that could only obscure dealing rationally with the epidemic and its victims.

"We found that the extreme positions of the left and right were inimical to progress within the commission," he said.

President Reagan has adopted a 10-point AIDS program that has included some of the commission's initiatives. A bill to be considered by the next Congress incorporates tougher protections for those afflicted by HIV; it also enjoys the support of President-elect Bush.

"Out in America we found an incredible group of human beings rising to oppose this tragedy," said Watkins. "Yes, it's a tragedy, but what an opportunity to deal with the complexities of society in a new way."

Watkins said a strategy for responding to AIDS, which will be left to the new Congress, the Bush administration and a new national AIDS commission, "is only a few percent of the solution. Implementation is the major work."

The cost of coping with AIDS is "hard to pluck out of the air," Watkins said, but he emphasized that no expense would be too high considering the price of doing nothing.

"[Cost] depends on too many complex factors," he said, "but if 4 to 7 ounces of prevention are still worth a pound of cure, then the costs are not that significant."

Noting that one estimate of the cost of a national AIDS program was \$3.1 billion per year, Watkins replied, "I come from [the Department of] Defense and I can tell you that figure is somewhat trivial."

"Human capital is our greatest resource," he stated. "Three billion dollars is a legitimate investment in a more wholesome, healthy society. We should all be willing to pay a lot more."

What would the money be spent on? Caring for those already ill, counseling those infected but not yet sick, educating people—particularly hard-to-reach populations (the so-called "underclass" that is four or five times more at risk of acquiring AIDS than the middle class)—about how to prevent AIDS, discovering how the AIDS virus works and funding basic research that can lead to clues in fighting human disease. Money would not be

spent on condoms and clean needles—issues irrelevant compared to the larger ones.

"We should be getting ready for the next mutant of HIV-1 (the scientific name of the agent that causes AIDS)," Watkins warned. "Will there be an airborne mutant in the future? We don't want to construct a Maginot Line against HIV-1 then wake up one morning and find HIV-3."

Watkins sees the AIDS crisis as an opportunity to revamp society in positive ways:

"We've never had an effective national health care policy in this country," he said; AIDS offers the chance to invent one;

AIDS demands that children of middle-school age learn "basic human biology, not just that of starfish and frogs";

AIDS also means coming to grips with the problems of an underclass numbering in the millions that is largely illiterate, impoverished and frequently ill.

"Nineteen eighty-eight could be the year that the United States decided to be a nation far more interested in serving others than itself," Watkins declared.

Those who argue that money to fight AIDS should not come from budgets such as defense were warned that "human potential in this country—not another aircraft carrier or a division of troops or another fighter wing—is the greatest factor in national security. All the chiefs (Joint Chiefs of Staff) will tell you that the number one readiness weight factor is people."

Among the people Watkins most lauded were NIH employees.

"NIH enjoys well-deserved credibility among the American people, on Capitol Hill and internationally," he said. "People look to you for sensible, logical recommendations."

Also speaking at the session were NIH director Dr. James Wyngaarden, who noted that NIH has spent almost \$1 billion so far on AIDS and plans to spend \$588 million in 1989; Dr. Robert Windom, DHHS assistant secretary for health, who noted that AIDS struck at a time when immunology was mature enough to recognize and begin to cope with it; Dr. Anthony Fauci, NIAID director, who thanked Watkins for emphasizing the role that undifferentiated basic research played in equipping medicine for the AIDS epidemic; and Dr. Carlyle Guerra de Macedo, director since 1982 of the Pan American Health Organization, a component of WHO.

"AIDS can bring us together or tear us apart, depending on how we meet the challenge," the Brazilian physician said.—Richard McManus □



Florence M. Shaw, a branch secretary in the NCI Office of Cancer Communications, recently won second prize in the Frederick County Fair for her embroidered quilt depicting the state birds. Shaw, who commutes daily to NIH from Frederick, worked on her quilt on and off for more than 5 years.

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Conference on Protein Conformation

An international conference on the "Experimental and Theoretical Aspects of the Interactions that Determine Protein Conformation" will be held in Masur Auditorium, Bldg. 10, Jan. 9-12.

The conference, sponsored by the Fogarty International Center and NIDDK, is open to the public and all interested scientists are invited to attend.

The folding of the polypeptide chain into a unique three-dimensional structure is the last stage in the translation of genetic information from DNA to a biologically active protein. This problem is a central one on the frontier of molecular biology; much experimental and theoretical effort is being devoted to understanding the folding process and to learning how to control and modify it (e.g., by site-directed mutagenesis).

The conference will bring together leading investigators in the field to exchange information and ideas. It has been organized by Drs. Harold Scheraga, professor of chemistry at Cornell University and Fogarty Scholar-in-Residence; Robert Jernigan, NCI; David Davies and Nancy Lamontagne, NIDDK.

For further information and registration please contact Agnes Hassan CSR, Incorporated, 1400 Eye Street, NW, Washington, DC 20005, 202/842-7600. □

Italian Buon Natale Festa

It's that special time of year when the aroma of homemade Italian treats pervades Bldg. 10—at least for a day. On Monday, Dec. 19, the sixth annual Buon Natale (Christmas) Festa sponsored by the NIH Chapter of the Order Sons of Italy in America will be held outside of Bldg. 10's second floor cafeteria during the lunchtime hours of 11:30 a.m. to 2 p.m.

Again this year, many of the delicious delicacies will be provided by the Italian embassy and the NIH Italian community. This year's festa will feature such Italian specialties as lasagne, torta rustica (cheese pie), Italian sausage sandwiches, Italian bread, cannoli and homemade desserts, etc. The proceeds of this event will help benefit the NIH patients in the Clinical Center. Due to the tremendous support of the NIH community to this special yearly event, the OSIA has been able to contribute thousands of dollars to the Friends of the Clinical Center and Patient Emergency Fund. So mark your calendars and plan to share with us in the spirit of this joyous holiday season! □



Graduating NIH and Presidential Management Interns are pictured with NIH associate director of administration John D. Maboney. They are (standing, l to r) Jan Kaplan, Joan Blair, Judy Gifford and (seated, l to r) Pat Turner and Victoria Putprush.

NIH Offers Opportunity for Career Change and Development

Are you interested in management careers in these areas: administrative services, budget, grants and contracts, personnel, program planning, or public information?

The NIH Management Intern Program has trained individuals demonstrating high potential for these careers and others and is now accepting applications for the FY 1989 program from Jan. 9 to Feb. 28. Past interns have come from a variety of backgrounds such as the nursing, biology, secretary and chemistry fields.

Application forms will be available beginning Jan. 9 in the NIH Training Center, DPM, Bldg. 31, Rm. B2C31. Applications must be complete and received by Feb. 19.

Information on the program, application

and selection process is provided at the following sessions:

Date	Building/Room
Jan. 11	Westwood/428
12	Parklawn/Conf. Rm. H
13	FCRF/Conf. Center Auditorium
17	31/Conf. Rm. 6
18	EPN/Conf. Rm. H
19*	10/9S235 (5:15—6:15 p.m.)
24	Federal/B1-19
25	10/9S235
26	36/1B13
27	HHS Bldg./703A

Sessions will be held from 11 a.m. to 12 noon except where noted by the asterisk.

For more information, please call the NIH Training Center, 496-6211. □

Middle-age Women Needed

The Unit of Peptide Studies, Biological Psychiatry Branch, NIMH is currently seeking female volunteers between the ages of 45 and 55 to participate in studies of menstrual cycle irregularity and the menopause.

Volunteers must be free of medical illnesses and not taking any medication on a regular basis.

Volunteers will complete daily rating forms and will be asked to participate in one of several protocols. Volunteers will be paid in accordance with the duration of each visit and the type of protocol.

For further information, contact Chris Hoban, 496-9675. □

Research Volunteers Needed

The Laboratory of Neurosciences at the National Institute on Aging is seeking healthy volunteers over the age of 40 for a study investigating the effects of aging on cerebral metabolism and cognitive functions. Participants must be drug-free during the study, and can receive a stipend of up to \$300 depending on the actual time involved. Call the laboratory, 496-4754, between 9 a.m. and 5 p.m., Monday through Friday for more information. □

McFARLAND

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handicapped. She is an EEO counselor and a member of the NCI EEO advisory group. When the Hispanic American advisory committee needed an NCI delegate to represent it, McFarland volunteered.

Her boss, Dr. Peter T. Mora of NCI's Division of Cancer Biology and Diagnosis, describes her as a "renaissance lady—a person whose constructive and positive attitude toward life is always advancing and changing for the better."

For the past several years, McFarland has taken a special interest in disadvantaged and minority students working in the laboratory, teaching them advanced techniques in biochemistry.

One student she likes to recall was a young Mexican-American woman from a poor family in New Mexico. McFarland spent the summer of 1980 teaching the young woman biochemistry and encouraging her to apply to medical school. The student later won a scholarship to the University of New Mexico Medical School and is now a physician.

One day a few years ago, a young Italian student with whom McFarland was working burst into tears and confided to McFarland that she "was in love and could not bear the thought of even a temporary separation" from her fiancé. McFarland confided the woman's



Vivian McFarland

distress to Mora, who arranged for the young woman's return to Milan. The student completed her studies, married her fiancé and is now working in cancer research in Italy.

Her current student, Richard McDonald, a 25-year-old graduate student from Howard University says: "Vivian McFarland teaches me things you can't find in books or at school. She has not only taught me to think like a better researcher, but she has made me a better person."

Her life's journey began 56 years ago in Bradenton, Fla., then a small town of four or five stores and a couple well-kept Victorian hotels on the Gulf Coast between Tampa and Sarasota.

When she was 12, McFarland worked on a gladiola farm shucking bulbs. But in high school, she became fascinated with the intricacies of chemistry. "Had I not had the vision to be a scientist, I might have ended up working in one of the citrus packing houses," she says.

Her abilities soon earned her a degree at Florida's A&M University in Tallahassee, where she majored in chemistry and minored in mathematics.

By fall 1954, McFarland had become an assistant instructor at A&M, teaching inorganic and analytical chemistry. In 1957, she joined the organic chemistry section of the Laboratory of Chemical Pharmacology at NCI. The laboratory synthesized polyglucose sulfate molecules that were being studied for their potential to kill cancer cells and viruses.

In 1965, with Mora, she isolated the intact nucleic acid from a mouse leukemia virus and in pioneering work showed that the single stranded RNA tumor viruses consist of a single molecule. The study of these RNA-containing tumor viruses preceded what is now known about retroviruses and oncogenes.

In 1980, McFarland with Dr. Krish Chandrasekaran showed that oncogenes appear early during the embryonic development of the cell. Their work appeared in *Science* and *Nature*.

McFarland now studies mouse cell lines and their interactions with viruses to determine the changes that occur when normal cells are transformed into cancerous ones. She has written and collaborated on 20 scientific articles.

Mora says she is a "superb methodologist and excellent biochemist who can perform any task given her, from recombinant DNA techniques to tissue culture."

She is also enthusiastic when she tells you she has raised seven children, and is president of the NIH Toastmasters Club and the NIH Yoga Club.

McFarland lives in Northwest Washington with her husband Marion, a former senior chief petty officer with the U.S. Navy who now works at George Washington University Medical Center. □

Carpoolers from Bowie/Annapolis

The Bethesda Ridesharing Office of the Montgomery Department of Transportation wants to locate NIH employees who commute from Bowie and Annapolis and are interested in vanpooling to the Bethesda area.

Interested NIH employees are encouraged to contact Larry Holman, NIH Parking Office, 496-6851, or Jennifer Myren, Bethesda Ridesharing Office, 656-5804. □

Gallo Gives Lecture Series

Dr. Robert C. Gallo, chief of the Laboratory of Tumor Cell Biology, NCI, delivered the Alix G. Mautner Lectures at UCLA on Nov. 15 and 16. This prestigious lecture series is given in memory of Alix G. Mautner, a graduate of UCLA and faculty member in the department of English at the time of her death in 1982.

Gallo also delivered "The Thirtieth Annual Bampton Lectures in America." This series of four distinguished lectures was held at Columbia University on Nov. 29 and 30 and Dec. 6 and 7.

Both series of lectures will be published as monographs. □

Cope with Holiday Stress

The holidays—Chanukah, Christmas, New Year's Day—are upon us. At this time of year, a shifting of gears takes place preparing us for the weeks to come. A transition in mood and spirit begins.

The holidays provide us with many rituals that help us cope with the end of the old year and prepare for the new year. Typically there is an array of demands associated with the holidays; admonitions to be happy, to make others happy, to be grateful, to make amends and to think about where we are going in our lives and where we have been.

When our outlook is positive, we look forward to the celebrations of the season. However when the evaluation is less positive, the holiday season can be quite painful. This is particularly true if some major losses have occurred; the death of a parent, the loss of a friendship, the ending of a marriage, the disappointment of a career reversal or the prospect of spending the holidays alone. The unfinished business of one's life has a way of resurfacing and demanding attention, adding a melancholy note to the end of the year. Even when life is going well, the sheer volume of demands may result in much stress. However, there are strategies for dealing with the stresses of the holiday season. Two essential starting points include recognition that the holiday season is a complicated time and willingness to maintain control by utilizing available resources. Such resources may include parents, spouse, children, friends, social groups and professional caregivers.

The holidays can be a time of reflection, joy, peace, love and happiness. If there is anything that is interfering with your enjoyment of the season, consider getting some help. The Employee Counseling Services is available to assist you in dealing with holiday stress. Contact Michael Bowler or Carol Weiss, 496-3164, for a confidential consultation. □



Dr. Christy Ludlow (l) directs Dr. Miboko Daito, who is administering an experimental therapy for the rare voice disorder spasmodic dysphonia.

NIDCD Scientist Gets Journal Award

After brilliance and technique, one could argue, a scientist's greatest asset is skill in communicating science. Dr. Christy Ludlow, chief of the intramural Speech and Voice Unit of the National Institute on Deafness and Other Communication Disorders, has recently been recognized for these qualities as the winner of the "Editor's Award as the 1987 Article of the Year."

Her paper, "Dynamic Aspects of Phonatory Control in Spasmodic Dysphonia," was chosen as the highest quality article of the year in the *Journal of Speech and Hearing Research*, the principal research journal of the American Speech-Language-Hearing Association (ASHA).

Ludlow was in Boston on Nov. 18 for the annual ASHA meeting, where she accepted the honor. "I was really surprised," she said. "I never even considered the possibility."

Nadine Connor, who is now at the University of Wisconsin-Madison, coauthored the winning article.—Kathy Kranzfelder □

Normal Volunteers Sought

The Laboratory of Socioenvironmental Studies, National Institute of Mental Health, is seeking healthy normal volunteers for a study of memory for textual material. Volunteers should be at least 18 years old, and should speak English as their first language. The study takes approximately 3 hours to complete; volunteers will be paid. Call Susan Levi or Leslie Caplan (496-3383) for further information. □

NIH Surpasses Dollar Goal

CFC Leader Curtis Wilburn Honored

"An enthusiastic team leader" are the words that come to mind when you first meet Curtis Wilburn, and that's exactly what his keyworkers thought of him during the 1988 Combined Federal Campaign (CFC).

He raised more than \$10,000 from the Division of Safety for this year's CFC. That's more than 140 percent over the goal set for the division. Curtis credits his keyworkers for helping him achieve that distinction as well as being the first coordinator to reach the individual BID dollar goal.

Curtis, property disposal specialist with the hazardous and solid waste management section, Environmental Protection Branch, Division of Safety, was chosen to organize 10 keyworkers in his division to canvass more than 200 employees. Many safety employees work all over the campus as well as a variety of shifts; each of Curtis' keyworkers visited every employee at least once during the campaign—not a small feat to do.

For his outstanding job with CFC this year, Curtis was awarded a certificate of appreciation from the director of the Division of Safety, Dr. Robert McKinney.—Susan Gerhold



Curtis Wilburn (r) accepts the congratulations of Division of Safety director Dr. Robert McKinney for raising more than \$10,000 from DS coworkers for the Combined Federal Campaign. Wilburn motivated 10 keyworkers to canvass more than 200 employees.



Ronald Gardner (l) has begun planning his trip after winning two free airline tickets from U.S. Air as part of a promotional prize for the 1988 Combined Federal Campaign. Pictured with Gardner are John Maboney, NIH associate director for administration (r) and Philip Amoruso, director of the office of administrative management, NCI. Gardner was one of many NIH'ers who contributed more than \$26 toward CFC this year. With contributions such as Gardner's, NIH for the first time ever exceeded its departmental goal and raised more than \$545,000. The BIDs can be proud, too; 16 BIDs out of 28 exceeded their individual goals as well. In the next few weeks, a victory celebration is being planned to celebrate NIH's successful 1988 campaign.



Bubbly 11 West patient Tommy Miles (c) hams it up for photos taken during the CFC drawing. Tommy picked Ron Gardner's name for two tickets on U.S. Air anywhere it flies as part of a promotion for CFC. Gardner was one of many who contributed \$26 or more to CFC during this year's campaign. Pictured with Tommy are Don Christoferson (l), deputy associate director for administrative management, NCI and John Maboney, NIH associate director for administration.

ANNIVERSARY*(Continued from Page 1)*

As the Hygienic Laboratory matured, its research interest broadened beyond infectious diseases. To reflect its expanded role, in 1930 the laboratory was renamed the National Institute of Health.

Nearly a decade later World War II began, and wartime needs directed the skills of NIH researchers toward military concerns: preventing disease among the troops, developing vaccines and sustaining the troops under the siege of tropical diseases. Wartime research resulted in an explosion of new medical knowledge, such as the development of life-saving treatments—penicillin, gamma globulin and cortisone. Laboratory technology flourished.

With the war's end, the nation's redirected energies were reflected in expanding resources for NIH. In 1948, this expansion resulted in reorganization. NIH's Division of Infectious Diseases itself became the core of an institute—the precursor to NIAID—that also incorporated the Division of Tropical Diseases, the Laboratory of Biologics Control and the Rocky Mountain Laboratory.

What's in a Name?—The New Institute

The new institute was called the National Microbiological Institute, reflecting its concern with all pathogenic organisms. Even the institute's first director, Dr. Victor H. Haas, referred to NMI as "a sort of orphan, an amorphous creation among the richer and more 'glamorous' categorical institutes" such as the National Heart Institute and the National Cancer Institute.

Yet during this period, NMI research blossomed. Among other notable accomplishments, vaccines against both rubella and adenovirus infections, the latter a serious problem among military recruits, were developed. Haas maintained this scientific impetus by establishing a new arm of the institute, the Extramural Research Branch, to fund research conducted outside of NIH and encourage young researchers through training and fellowship grants.

But NMI continued to suffer an identity crisis. It was clear that the institute's potential had expanded beyond studies of organism classification and human response to infection. In early work on developing diphtheria and tetanus antisera, scientists observed that some patients exhibited severe hypersensitivity reactions to horse-serum injections. The existence of this sort of response—the immune system gone awry—indicated that basic research on the immune system needed to be incorporated into the institute's future plans.

To acknowledge NMI's expanded mission,

it was renamed the National Institute of Allergy and Infectious Disease in 1955. The word "allergy" was understood in a broad sense to represent the study of immunology, then a fledgling field of science.

NIAID's Leaders Shape the Institute

After Haas set the initial course for the institute's programs, each subsequent director's accomplishments were molded by his own goals combined with the technology of the times. By reviewing notable accomplishments of each director's tenure, one can chart the institute's evolution.

1957–1964 Under the leadership of Dr. Justin M. Andrews, new findings—particularly studies of viruses causing flu, colds, tumors and epidemic acute respiratory disease in humans—dramatically advanced efforts to conquer infectious diseases. The institute initiated nationwide projects to promote research in infectious diseases, vaccine development, antiviral drugs and transplantation immunology. "Our traditions have been established," said Andrews. "We need only maintain them and we shall achieve our purposes." With the Walter Reed Army Research Institute, NIAID also set up the Middle America Research Unit to study tropical and parasitic diseases in the Canal Zone.

1964–1975 Cellular immunology, which came to the forefront during the directorship of Dr. Dorland J. Davis, offered new ways to study various disorders. Davis established the first allergic disease centers, which translate basic research into experimental treatments. He also established the first research centers for the study of sexually transmitted diseases and of influenza. In 1968, NIH transferred to NIAID two international research programs: the U.S.-Japan Cooperative Medical Science Program, set up to explore health problems in Asia; and the International Centers for Medical Research and Training, an initiative to broaden the scope of U.S. health sciences through international research.

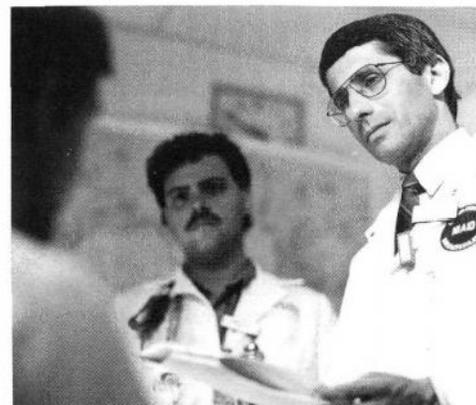
1975–1984 NIAID continued to expand under the leadership of Dr. Richard M. Krause. During this time, an explosion of new scientific knowledge occurred in both immunology and molecular biology, and biotechnology burst upon the scene. These advances allowed NIAID to expand its clinical programs in immunology and increase research in bacterial and viral pathogenesis. The institute also led the way in recombinant DNA research and supported construction of the first U.S. maximum containment facility for this research in Frederick, Md.

1984–present Acquired immunodeficiency syndrome (AIDS), an infectious disease that attacks the immune system, was already mushrooming into a new global epidemic

when Dr. Anthony S. Fauci became director of the institute in 1984. Then, fewer than 7,000 Americans had been diagnosed with AIDS; today, that number has increased more than tenfold. AIDS research now commands nearly 50 percent of NIAID's budget. To the thousands of AIDS researchers working in clinics and laboratories, many funded by NIAID, AIDS is both a pressing medical problem and a labyrinthine scientific mystery.

Largely as a result of the urgent AIDS situation, NIAID has grown in 4 years from the seventh largest NIH institute to the third largest one in terms of budget, and the second largest one in terms of personnel.

While the development of the AIDS research effort itself has been remarkable, other areas of NIAID research have blossomed



Dr. Anthony S. Fauci, NIAID director and chief of the Laboratory of Immunoregulation, goes over details of vaccine protocol with prospective volunteer. NIAID nurse Frank Cefali is in background.

in their own right as well as benefitted from the AIDS effort. Immunology's role in myriad infectious diseases is becoming better understood. Spinoffs of AIDS research are being applied in the fields of molecular biology, bone marrow transplantation, vaccine and drug development and the design of clinical trials.

In addition, the institute has recently increased its commitment to research on sexually transmitted diseases other than AIDS and to research in transplantation immunology.

Looking Toward the Future

After 40 years, NIAID retains its youthful energy in the face of the fast-changing world of medical science. In the words of Fauci, "Challenges abound as we encounter such new problems as drug resistance in malaria, the epidemic of sexually transmitted diseases and the emergence of a deadly new disease—AIDS. Medical scientists have a keen awareness of the

magnitude of human suffering caused by infectious and immunologic diseases and the great need for better ways to diagnose, treat and prevent these illnesses.

"We also have great confidence that the rapidly burgeoning fields of immunology, cell biology and molecular genetics and the concurrent revolution in biotechnology have brought us to the edge of discovery of new answers to many medical problems.

"In our search for research results that have immediate clinical application, however, we cannot overstate the intrinsic value of basic research. The history of science continually proves the far-reaching influence of researchers who are free to exercise their intellect, curiosity and imagination in the pursuit of new scientific truths." No single tenet better describes the inspiration guiding the past four and many future decades of NIAID research.

Biomedical Detective Identifies Elusive Agent

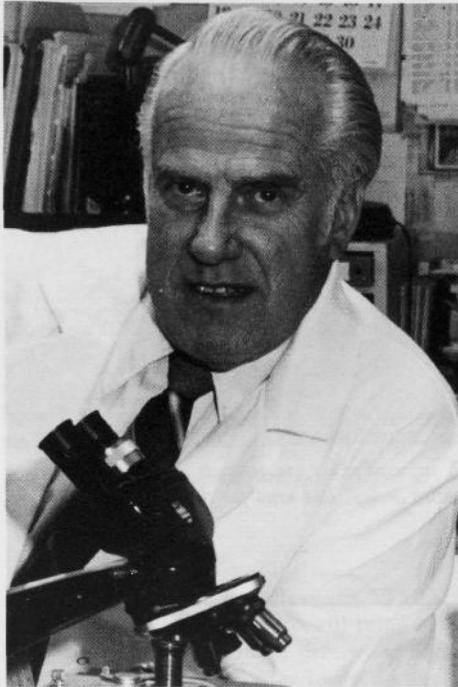
NIAID's Rocky Mountain Laboratories

For scientists in basic research, there are few "eurekas." Piece by piece, researchers seek out tantalizing bits of evidence that eventually might prove to be a solid clue. At NIAID's Rocky Mountain Laboratories (RML), one of these biomedical sleuths has received international recognition for his successful detective work in solving a medical mystery that has become an increasing health concern in America—Lyme disease.

Situated in Montana's lush Bitterroot Valley, RML came into being because of an earlier medical puzzle. Many of the early settlers attracted to the fertile valley were plagued by a disease they knew as "black measles" or "spotted fever." In 1902, the U.S. Public Health Service sent out a research team to find the cause. Tents, cabins and an old schoolhouse were used for housing the early labs, where the researchers ultimately not only identified the source of the problem—tick bites—but also formulated a vaccine against the agent. In gratitude, the State of Montana built the present facilities, which the Public Health Service then purchased in 1931. With the NIH reorganization 40 years ago, the laboratories became a component of the new Microbiological Institute, NIAID's precursor.

The 41 scientists now at RML continue research on arthropod-borne diseases in addition to studying animal infections transmissible to humans, slow-virus diseases, vaccine development, and more recently, the acquired immunodeficiency syndrome (AIDS). The following story depicts the kind of work conducted at RML.

In 1975, the Connecticut State Health



Dr. Willy Burgdorfer

Department received a phone call from a mother concerned about the outbreak of a strange disease in her village. Twelve children had been affected. Local doctors had diagnosed the disease as juvenile arthritis.

Soon after, another woman in the same locality contacted a clinic at Yale Medical School about an "epidemic" of arthritis in her family. Subsequent investigations showed that the clinical and epidemiologic patterns were the same in both outbreaks. Because the disease seemed to be unique to this general locality and was first identified in a village called Lyme, it came to be known as Lyme disease.

From 1975 to 1979, Connecticut health officers recorded 512 cases of Lyme disease. Further epidemiologic and ecological studies, funded by another NIH institute, incriminated a tiny tick, which lives off rodents and white-tailed deer, as the carrier of the disease. Yet the microbe that actually causes Lyme disease remained unknown.

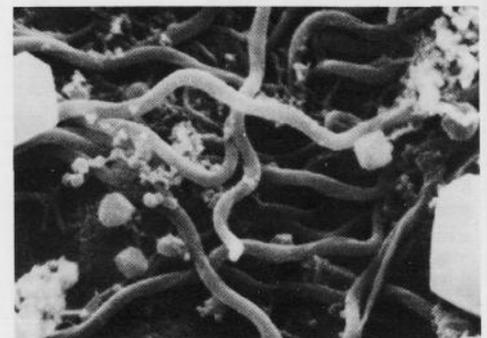
Meanwhile, back at RML in Montana, Dr. Willy Burgdorfer, a pathobiologist specializing in tick-borne diseases, was continuing his work in Rocky Mountain spotted fever. He had become interested in spotted fever cases occurring in New York, among residents of Long Island. Is it possible, he wondered, that the Rocky Mountain spotted fever bacterium, *Rickettsia rickettsii*, is transmitted by the deer tick?

With his collaborator, Dr. Jorge Benach from the New York State Department of

Health, Burgdorfer had examined several hundred ticks, but saw no evidence of rickettsial infection. Then, in September 1981, Burgdorfer received one additional shipment of ticks for testing. While examining the tick blood for rickettsiae, he found what looked like microscopic worms. In hot pursuit, hoping to learn more about these worms, he dissected the ticks and prepared smears from the removed tissue.

He did not find what he had expected. Instead, his microscope revealed spirochetes—the same spiral-shaped microbes later detected in Lyme disease patients. In addition, spirochetes he subsequently isolated from European ticks were identical to the Lyme agents. Since the turn of the century, European doctors had been diagnosing another tick-borne disease they called erythema chronicum migrans (ECM). Burgdorfer showed that Lyme disease is actually a severe form of ECM. The mystery was solved.

In the annals of science, one of the highest forms of recognition is naming an organism for the investigator who discovered it. In the ancient taxonomic tradition, therefore, the spirochetes that cause Lyme disease are now known as *Borrelia burgdorferi*. For his discovery, Burgdorfer was also awarded the Schaudinn-Hoffman plaque by the German Society of Dermatologists during its 34th congress in Zurich, Switzerland in 1984. Schaudinn and Hoffman, in 1903, discovered *Treponema pallidum*, the organism that causes syphilis. Further kudos came last year from Switzerland, where the University of Bern presented Burgdorfer with an honorary medical degree in recognition of his spirochete work;



An electron microscope yields a view of *Borrelia burgdorferi*; in the midgut of a tick. The organism causes Lyme disease.

this past month, the West German Minister of Health presented Burgdorfer with the prestigious Robert Koch Foundation Award.

For the true scientist, however, an answer only stimulates more questions. Doctors now know how to treat Lyme disease, but diagnos-

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ing the disease remains difficult. Not only are its symptoms similar to those of other diseases, the diagnostic blood tests presently available are not reliable. Several years ago, Burgdorfer devised a quick test for identifying ticks infected with spotted fever rickettsiae. Now, in collaboration with other RML researchers, he is working to improve the diagnostic tests for Lyme disease.

In the isolated Montana laboratories, Burgdorfer continues in his role as a biomedical Sherlock Holmes—even though he officially retired in 1986. It seems particularly fitting to profile Burgdorfer as NIAID celebrates its 40th anniversary because his NIAID career, which began in 1951, has very nearly spanned the life of the institute.—Karen Leighty



A ragweed plant can generate a million grains of pollen a day, bad news for those allergic to it.

Research on Allergies

More than 35 million Americans suffer from allergies. Most have hay fever or allergic rhinitis. Asthma, too, is often caused by allergies, making it the second most common allergic disease. Millions more Americans have allergic reactions to substances such as dust, molds, medicines, insects, foods and dyes. Surprisingly, NIAID researchers recently found that some women are even allergic to their own hormones.

But what is an allergy? An allergy is an altered immune response to a substance that is usually benign. Allergy symptoms range from mild although uncomfortable, like the itchy eyes and sneezing of the hay fever sufferer, to life-threatening, as in the case of a person who goes into anaphylactic shock after a bee sting.

Research on allergic diseases has been part of NIAID's mission since it was established as the National Microbiological Institute in 1948. The increasing importance of allergy research was recognized by Congress in 1955 when it authorized NIH to change the institute's name to the National Institute of Allergy and Infectious Diseases. The term allergy was understood to include the then embryonic field of immunology.

The close link between allergy and immunology research crystallized in 1967 when an extremely important discovery was made. Drs. Kimishige and Teruko Ishizaka, an NIAID-supported husband-and-wife team at Johns Hopkins University, identified a new class of protective proteins called IgE. The discovery of the IgE antibody opened a new era of research into hypersensitivity or allergic reactions and has led to better ways to approach the diagnosis and treatment of allergic patients.

When an allergen (allergy-inducing substance) such as pollen enters the body, special cells carrying IgE antibodies on their surfaces release chemical mediators such as histamine. These mediators activate the immune system, causing the allergic reaction. The IgE-carrying cells, known as mast cells and basophils, have proven to be key players in the allergic reaction.

Since IgE antibody was identified, scientists have continued to try to define exactly how the molecule works by looking at the products of cellular secretion that act together to decrease or increase IgE production. Their findings continue to improve methods of immunotherapy, also known as allergy shots.

The discovery of IgE led to the establishment of two exciting and innovative allergy research programs in the 1970's. The first, the Allergic Disease Centers (now called Asthma and Allergic Diseases Centers, or AADCs), were organized in 1971. NIAID established

Highlights of NIAID Accomplishments

The National Institute of Allergy and Infectious Diseases supports basic and clinical studies in immunologic, allergic and infectious diseases. For the past 40 years, NIAID-supported scientists in Bethesda and at other institutions across the country have contributed significantly to our knowledge in these areas to the benefit of public health. A representative list of accomplishments, by no means inclusive, follows.

Immunology

- Elucidated the roles of T and B cells as key players in the immune response. Described how the thymus acts as a factory for T-cell production.
- Showed how the body can produce a seemingly endless number of antibodies (infection-fighting proteins), each of which is generated in response to a specific foreign substance or microbe. Elucidated the molecular structure of antibodies.
- Developed a tissue-typing technique that made possible the first bone marrow transplant between persons other than identical twins.
- Performed the first successful procedure for treating human graft-vs-host disease, in which the body rejects transplanted tissue.
- Developed a successful treatment for once-deadly inflammatory diseases, particularly the vasculitic syndromes such as Wegener's granulomatosis, an inflammation of the blood vessels, lungs and airways.

Allergy

- Identified immunoglobulin E as the factor responsible for immediate hypersensitivity in

allergic reactions.

- Identified leukotrienes and other chemicals produced by the body as causes of allergic reactions.
- Described how late-phase allergic reactions can cause delayed-onset asthma, which has led to new approaches to asthma therapy.

Infectious Diseases

- Identified or isolated the infectious agents responsible for Lyme disease, hepatitis A, histoplasmosis, mycoplasmal pneumonia, rotavirus diarrhea, Rocky Mountain spotted fever and respiratory infections caused by parainfluenza viruses and respiratory syncytial virus.
- Established the role of sexually transmitted chlamydial infection in conjunctivitis (inflammation of the eye), pneumonia in newborns and pelvic inflammatory disease as well as the role of toxoplasmosis in eye disease. Developed with the drug manufacturer an antiviral treatment regimen that suppresses and prevents frequent recurrences of genital herpes.
- Developed new or improved vaccines for rabies, rubella, influenza, hepatitis B, pneumococcal pneumonia, *Haemophilus influenzae* type B meningitis and adenovirus-caused severe acute respiratory disease.
- Began the first U.S. testing in humans of an experimental AIDS vaccine.

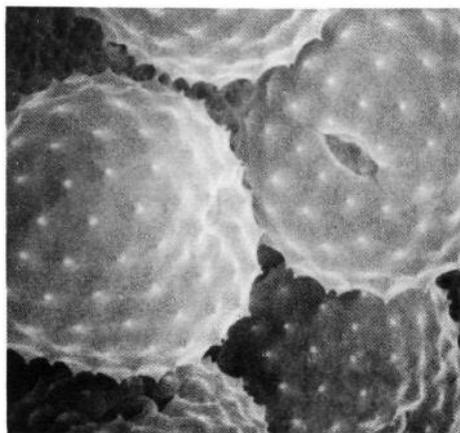
12 AADCs across the nation to foster collaboration between clinical allergists and basic research immunologists and geneticists, biochemists and pharmacologists.

Several years later, a program complementary to AADC, the Centers for Interdisciplinary Research on Immunologic Diseases (CIRIDs), was established by Congress. The six university-based CIRIDs help speed the application of new findings about the immune system to clinical problems in asthma and allergy as well as other immunologic diseases. The CIRIDs also conduct outreach activities within their communities to further translation of research findings to clinical practice.

Under the direction of NIAID's Allergy, Immunology, and Transplantation Program, these centers have greatly increased scientific knowledge about the mechanisms of allergic reactions. In particular, immunopharmacology, the study of the effects of drugs on the immune system, has played a major role in research to prevent and treat allergic diseases. In addition, scientists have increased their understanding of how chemical mediators cause inflammation and of how the cells that produce these mediators function. Pharmaceutical chemists are designing drugs that will prevent or treat the reactions of the immune system to allergens and continue to study the precise chemistry of allergies so that these new drugs will not themselves cause an allergic reaction.

Increased understanding of the mechanisms of allergic diseases has led to the development of new drugs within the last 15 years that have dramatically improved the lives of allergy and asthma sufferers. Among the most important additions to therapy are steroid nasal sprays and inhalers. These drugs reduce nasal swelling and inflammation, and mucus production. In addition, they boost the effectiveness of other asthma medications. Cromolyn sodium, which inhibits the release of histamine, is a powerful drug that prevents allergy symptoms. Also new on the market are improved antihistamines that don't cause drowsiness. Recently introduced bronchodilators allow asthma patients, especially those with exercise-induced asthma, to breathe easier by opening up the airways.

One growing area of concern is allergy in the workplace. Some people develop allergies to substances that they work with, such as metals, chemicals, grain dust or flour. These occupational allergies cost employees millions of dollars in lost wages each year. By studying genetic markers—certain identifiable inherited characteristics—NIAID researchers hope to be able to predict before symptoms appear who is at high risk of developing an allergy in certain occupational settings and in other settings as well.



These ambrosia ragweed pollen grains, magnified 3,000 times, look somewhat sinister, at least to sufferers of hay fever.

Continuing collaboration between NIAID researchers and other scientists will bring about even better methods of preventing and controlling allergic diseases and help doctors help the millions who suffer from allergic diseases lead lives free from the debilitation these disorders bring.—Ann C. London

NIAID AIDS Research

The laboratory technician recalled the day clearly—the day 7 years ago when Dr. Anthony S. Fauci, now director of NIAID, called her and other members of his laboratory into his office. In a quiet, serious manner, Fauci opened his file drawer and pulled out two scientific reprints. The articles reported that Kaposi's sarcoma, a rare form of cancer, and *Pneumocystis carinii* pneumonia, a rare infectious disease, were striking down young, previously healthy homosexual males. In addition, blood tests on each patient showed that their T cells, white blood cells that help the immune system defend the body against foreign invaders, either were unable to fight the invaders or were destroyed. Fauci was particularly intrigued by these latter findings because as chief of NIAID's Laboratory of Immunoregulation, he and members of his lab had been studying T cells and their role in the immune system.

These first cases of the acquired immunodeficiency syndrome (AIDS) were reported by the Centers for Disease Control in 1981. Even during those early days of what is now a global pandemic, Fauci instinctively felt that the disease would have a major impact on public health. As he wrote in an editorial to the *Annals of Internal Medicine* in early 1982 "... the immediate goal that must be recognized and vigorously pursued is the designation of resources and energy to the

solving of the mystery behind this extraordinary disease"

In 1986 NIAID established the Acquired Immunodeficiency Syndrome Program (AIDSP). Beginning with a staff of five, the AIDS Program was charged with initiating and coordinating NIAID extramural research on AIDS and HIV.

Within the first 6 months, the program had funded 14 AIDS Treatment Evaluation Units in university-based medical centers to conduct clinical trials of therapeutic agents. Shortly after these units were established and while protocols for the first studies were being developed, an exciting and unexpected occurrence dramatically changed the nature of placebo-controlled clinical trials for AIDS patients.

In September 1986, a drug company-sponsored clinical trial of the antiviral drug AZT was prematurely halted when a Data and Safety Monitoring Board determined that AZT had indeed been improving and prolonging life for AIDS patients who had had *Pneumocystis carinii* pneumonia. The board recommended that the drug be given to other patients who might benefit. This exciting news gave people with AIDS a glimmer of hope in their life-and-death struggle with this disease.

The AIDS Program staff turned its energies to setting up a distribution system so that AZT could be given to eligible patients. Working in collaboration with the National Cancer Institute and Burroughs Wellcome Co., makers of AZT, NIAID staff arranged for more than 4,200 patients to receive AZT under a Treatment IND granted by the Food and Drug Administration.

The recognition of the benefits of AZT also meant that this drug would play a major role in future clinical trials of anti-HIV agents. Protocols already under development for the new ATEU program had to be revised to reflect these new results.

Within the first year of operation, the number of ATEUs increased to 19. Since that time, the clinical trials program has continued to expand. Now called ACTUs or AIDS Clinical Trials Units, they number 45, including 13 pediatric units, and are part of a collaborative AIDS Clinical Trials Group. Approximately 5,000 patients have enrolled in ACTG clinical studies.

A part of this search for effective therapies includes targeted drug development efforts. Through the National Cooperative Drug Discovery Groups, top scientists from academia, industry and government are working together to identify and develop, through preclinical testing, new drugs for HIV infection. Three drugs have already been discovered and developed through the program. A genetically

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engineered form of soluble CD4 entered clinical trials earlier this year. Two potentially promising drugs, nucleotide analogs D4T and AZDU, are expected to enter clinical trials in early 1989. Many other drugs are in earlier stages of preclinical evaluation and testing.

Collaborative vaccine development groups have also been established to develop new approaches to AIDS vaccines. In 1987, safety tests of the first candidate human AIDS vaccine began at NIAID. This vaccine as well as a second product are now also being tested in six NIAID-supported Vaccine Evaluation Units.

AIDSP has recently initiated an innovative program, the Community Programs for Clinical Research on AIDS, that will involve community physicians in AIDS research. By including primary care physicians in AIDS research, NIAID hopes to involve in clinical trials more HIV-infected black and Hispanic persons and intravenous drug users as well as more women at risk of HIV infection. Participants in this program may be individual and group health care providers, public and private clinics, community organizations, and hospitals that may have no prior experience in conducting clinical trials.

AIDS research is also a top priority in NIAID laboratories. The NIAID Intramural Research Program is exploring exciting areas such as vaccine research and development, the pathogenesis of HIV infection and AIDS, and the development of animal models such as rabbits and transgenic mice. Investigators are looking for improved treatments and better diagnostic methods as well as studying the role of other infectious agents in the development of HIV infection. NIAID researchers collaborate with scientists in other institutes at NIH and with scientists outside NIH.

The institute's response to the public health crisis presented by this new disease has been extraordinary. In dealing with this crisis, scientists have learned a remarkable amount about AIDS and HIV infection within a relatively short period of time and, equally important, they have tremendously increased their knowledge about the human immune system. This increasing knowledge will help researchers as they struggle to find treatments and a possible cure for AIDS and HIV infection as well as for other infectious diseases.—Ann C. London

Antiviral Drug Research

Viruses cause the most common acute infectious illnesses in the United States and are responsible for a number of persistent infections. New viruses that cause diseases ranging in severity from mild to lethal continue to be discovered. Furthermore, there is mounting evidence that viruses have a role in certain chronic diseases. Thus the need for effective drugs for the treatment and prevention of viral diseases has assumed growing importance.

Very few drugs have been found that will destroy or inhibit the growth of viruses without also destroying host cells. However, scientists have devised new approaches based on advances in the scientific understanding of the molecular biology of virus replication. It is now theoretically possible to design antiviral compounds that act directly or indirectly on the biosynthesis or replication of the viral genome. Most of the currently available agents are quite toxic and can be used clinically only under certain limited circumstances. NIAID is emphasizing research on the development and testing of new, targeted antiviral agents that will interfere with viral pathogenicity but will have minimal deleterious effects on the host cell. In addition, the efficacy of biological response modifiers such as interleukin-2 and the interferons is being evaluated.

Two main approaches are used to develop new antiviral drugs. One, the empirical approach, involves screening existing compounds for antiviral activity. The other, the rational approach, involves designing new compounds to interfere specifically with known mechanisms of viral replication and pathogenesis (destructive effects of viral infection). The rational approach enables scientists to develop antiviral drugs that target mechanisms used exclusively or selectively by viruses and are therefore not expected to harm human cells.

NIAID intramural and extramural programs have had a long-standing interest in antiviral research at three levels: basic, preclinical and clinical. Through the Microbiology and Infectious Diseases Program (MIDP), NIAID supports a number of basic researchers who are applying detailed molecular knowledge of viral mechanisms of infection and pathogenesis to the development of innovative approaches to creating antiviral drugs. The intent is to stimulate basic research in promising areas of antiviral drug development that industry may be unwilling to pursue.

Preclinical evaluation studies focus on animal model systems that mimic disease processes in humans. MIDP supports research on the development of animal models of various human diseases, including varicella, cytomegalovirus infection, herpes, AIDS and influenza. These models provide a ready mech-

anism for the screening and evaluation of new antiviral drugs prior to clinical trials.

NIAID-supported researchers are also pursuing the clinical evaluation of antiviral substances. The NIAID Collaborative Antiviral Study Group (CASG) embraces a large number of university-based research projects that have tested drugs against various viral diseases, including herpes simplex encephalitis, neonatal herpes infection and herpes zoster.

Studies by CASG researchers showed for the first time the clinical value of a systemic antiviral agent, vidarabine, against a serious viral disease, herpes simplex encephalitis (HSE). A rare complication of herpes simplex infection, HSE, if left untreated, kills more than 70 percent of patients and leaves few survivors with normal neurologic function. Subsequently, a CASG study showed that acyclovir, a drug recently licensed for treatment of genital herpes, offers significant advantages over vidarabine. It reduces mortality and increases the percentage of patients who ultimately either return to normal function or have manageable impairment.

They are also studying the use of acyclovir against neonatal herpes infections. The disease, which occurs in infants born to mothers with genital herpes, affects 1,000 babies each year in the United States. Neonatal herpes can affect the central nervous system, leading to mental retardation or death. Recent studies have documented the essential equivalence of acyclovir and vidarabine for treatment of neonatal herpes infections.

Herpes zoster, or shingles, is caused by varicella zoster virus, which also causes chickenpox. In immunocompromised patients, the disease can become disseminated and threaten life. Herpes zoster also affects healthy people, primarily the elderly, and can be very painful. NIAID-supported researchers are comparing treatment with acyclovir or steroids, or a combination of the two, to promote healing and reduce pain.

Oral acyclovir was also shown by NIAID intramural and extramural scientists to treat genital herpes, a disease affecting 30 million Americans, effectively. In later studies, they showed that daily use can prevent most recurrences.

Based in part on NIAID-supported research, alpha interferon has been approved for the treatment of genital warts, an increasingly prevalent sexually transmitted disease. Experimental therapies involving interferons continue to be evaluated for two types of papillomavirus infections, laryngeal papillomatosis in children and genital warts in adults.

NIAID-supported investigators have analyzed the mechanisms of action of two drugs, amantadine and rimantadine, that can prevent and treat influenza A infections. Amantadine

has been licensed for use, and the effectiveness of rimantadine has also been demonstrated.

These and many other studies of antiviral drugs lead scientists to hope that one day viral illnesses may be as treatable as many bacterial infections are today.

The War on Infectious Diseases

Three years after World War II ended, NIAID came into being as the National Microbiological Institute (NMI). As one battle was winding down, a longer-standing one—the battle against infectious diseases—was picking up new vigor.

The most frightening disease in America throughout the 1940's was polio. But following the conquest of polio, which occurred during the next decade, widespread respiratory, gastrointestinal and liver diseases became increasingly recognized as important causes of sickness and death. The agents of these diseases were thought to be viruses but had yet to be identified. Remarkable progress in discovering the causes of these illnesses and developing vaccines and treatments to combat them was made by scientists in the new NMI and its successor, NIAID.

Respiratory Diseases

In the early 1950's, scientists in NIAID's Laboratory of Infectious Diseases (LID) first identified and characterized a family of viruses, called adenoviruses, linked to epidemic outbreaks of debilitating coughs and fevers among infants, children and military recruits. Other LID investigators later designed a novel live adenovirus vaccine now routinely used in the military. The oral vaccine has a special coating allowing it to be released only after it reaches the intestines. The vaccine thus bypasses the upper respiratory tract, where it ordinarily produces disease, and then proceeds to cause a silent infection confined to the intestines, where it stimulates immunity.

Around the same time, LID scientists discovered the nature of the agent that causes what was then called atypical (non-bacterial) pneumonia, thereby solving what was at that time one of the most perplexing mysteries of clinical microbiology. Surprisingly, they found that the agent was not a virus but a similarly small organism called a mycoplasma, a rudimentary bacterium lacking a cell wall. Failure of the disease to respond to penicillin or sulfa drugs used to treat bacterial pneumonia had been one of the initial clues that this was an unusual type of pneumonia. Following identification of the disease agent, large-scale clinical trials conducted by these scientists revealed that patients treated with tetracycline recovered rapidly from the disease.

In the late 1960's, with measles, mumps and rubella now preventable, NIAID assigned a high priority to research on serious respiratory infections of children. All types of respiratory syncytial virus (RSV) and parainfluenza viruses known to infect humans were subsequently first identified and characterized by LID scientists. RSV—the most important cause of pneumonia during infancy and early childhood—is unique among the many human viruses because of its particular impact and virulence during the earliest months of life. Parainfluenza viruses are the most common cause of croup. Efforts to develop vaccines for these two groups of viruses continue.

At the other end of the age spectrum, influenza virus can cause severe disease in the elderly and those with chronic diseases, people whose immune systems are naturally weakened by age or illness. Through the use of non-human viruses, the "Jennerian" approach to vaccination, LID scientists recently developed a successful experimental vaccine against influenza A. They first identified several influenza A viruses of birds that were attenuated, or weakened, for monkeys. Then they transferred the avian influenza virus genes responsible for this attenuation into a hybrid virus containing the protective antigens of a human influenza strain. This resulted in the development of an experimental live vaccine that promises to be more effective than the current inactive vaccine.

Diarrheal Diseases

In the 1970's, LID launched a major research effort to find viruses that cause gastroenteritis, inflammation of the stomach and intestines. The modern era of gastroenteritis virology dates back precisely to the first studies in LID of what was then erroneously called intestinal flu. It was found that this acute illness is actually caused by a group of small viruses that infect the intestinal tract. LID scientists employed immune electron microscopy (IEM)—a technique that permits visualization of virus particles present in very small amounts in specimens—to characterize the first of these viruses, the Norwalk virus. This was the first time IEM had been used to detect a previously unrecognized viral pathogen. This discovery laid the groundwork for the subsequent visualization by IEM of hepatitis A virus. Norwalk virus remains the most important cause of epidemic viral enteritis, causing 30 percent of outbreaks in families or large groups of people exposed to contaminated food or water.

Subsequently, while searching for Norwalk virus in stool samples of children with life-threatening diarrhea, LID scientists identified a slightly larger, wheel-shaped virus, designated rotavirus. Rotavirus is now known to

cause about half of all serious diarrheal diseases in infants and young children throughout the world. In developing countries diarrhea causes 15 to 30 percent of all deaths, many in children under 2 years of age. LID scientists have developed a promising live rotavirus vaccine now undergoing field tests in five countries.

Hepatitis and AIDS

Few areas of infectious disease research have grown as fast as hepatitis research. Twenty years ago, none of the hepatitis viruses had been identified. Of the five viruses now known to cause hepatitis—A, B, non-A, non-B (blood-borne), non-A, non-B (epidemic), and delta—four were either isolated or initially characterized by LID scientists. Liver damage caused by chronic infection with certain hepatitis viruses, especially hepatitis B, is a major global health problem. LID scientists provided the first evidence that a highly purified surface antigen of hepatitis B virus (HBV) induced complete resistance to HBV in the chimpanzee, an observation that was critical to the successful development of an HBV vaccine. LID scientists are working on new and improved vaccines against both HBV and hepatitis A virus.

Most recently, LID scientists have been intensively studying AIDS-related viruses that infect monkeys and cats, using these viruses and their animal hosts as models for the human disease. "Scientifically, AIDS has broken several major rules of virology," comments Dr. Robert M. Chanock, chief of LID for the past 20 years. For example, neutralizing antibodies to the AIDS virus do not seem to provide effective immunity to infection. In a study by researchers in New York, chimpanzees passively transfused with large amounts of antibodies were not protected against a very small challenge with the AIDS virus. Usually if a person has antibody, he or she is protected against serious disease caused by a virus that disseminates throughout the body. "How the AIDS virus evades the host immune system is one of our major concerns," says Chanock.

New Technology

Fortunately, the tools scientists have to work with have been evolving rapidly, speeding up the research process. Genetic engineering has transformed vaccine research from unsophisticated shotgun science to an elegant art. Says Chanock, "Twenty years ago we were seeking mutant viruses for use in vaccines by putting tremendous pressure on the virus, exposing it to mutagens or to other selective pressures and seeing what happened. We were limited, though, both by the type of mutation induced by the chemical mutagen

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we used and by our ability to identify that mutant if it did exist; if it was a minor component in the total population, we had to try to fish it out of the mixture of viruses."

Recombinant DNA technology has now made it possible to dissect a virus, to determine which parts of the virus help cause disease and which parts confer protective immunity. "In many circumstances, scientists can now design organisms to their specifications. It's opened up new avenues of research," comments Chanock. "Investigators can work much more efficiently, much more effectively, and with greater promise of success."

The new biomedical technology, including monoclonal antibodies, has also enabled scientists to map all the antigenic sites on a virus and to determine which few are points of vulnerability, sites that bind neutralizing antibody.

Even with these remarkable leaps forward, many problems in infectious disease research remain. And as recent history has proved with Legionnaire's disease, toxic shock syndrome, Lyme disease, and now AIDS, scientists must be ever-vigilant because infectious agents can appear from out of the blue to pose serious new health problems.

On the other hand, by manipulating viruses scientists have learned that viruses harbor great potential to serve as well as harm us. Already vaccinia virus and adenovirus, once the virologist's enemies, have been reincarnated to carry foreign genes for new-generation vaccines. NIAID scientists developed the recombinant vaccinia virus vector now being used as the basis for an experimental human AIDS vaccine. A portion of the DNA of dengue virus, a major health problem in tropical and semitropical countries, has also been inserted into vaccinia virus for testing as an experimental vaccine in animals. Such approaches couldn't have been dreamed of by scientists 20 or 40 years ago. It's likely that as we ease into the next century, new biomedical challenges and new scientific tools to combat them will make the infectious diseases research of tomorrow equally exciting, important and unpredictable.—Laurie K. Doepel

Lecture on Eating Disorders

The NIH Employee Counseling Services will present a lecture on "The Hungry Heart: A Look at Eating Disorders," presented by Monica Callahan, on Wednesday, Jan. 11, 1989, at noon in Wilson Hall, Bldg. 1. □



TRAINING TIPS

The NIH Training Center of the Division of Personnel Management offers the following:

<i>Courses and Programs</i>	<i>Dates</i>
<i>Management and Supervisory 496-6371</i>	
Positive Influence and Negotiation	1/25
Time Management	1/10
Pragmatic Problem Solving	1/18
How to Write and Publish Scientific Papers	1/23
Getting Results in Task Oriented Groups	2/15
Attitudes: How They Affect the Work Environment	2/7
Creative Basics for Changing Workplaces	2/10
Effective Presentation Skills	2/13
Federal Budget Process	2/22

Office Operations Training 496-6211

Adult Education 496-6211

Training and Development Services 496-6211 (TDSP Registration started Dec. 5)

Management Intern Applications (496-6211) will be available Jan. 9, 1989

Personal Computer training is available through User Resource Center (URC) self study courses. There is no cost to NIH employees for these hands-on sessions. The URC hours are:
Monday–Thursday 8:30 a.m.–9:30 p.m.
Friday 8:30 a.m.–4:30 p.m.
Saturday 9:00 a.m.–3:00 p.m.

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Of Music and Madrigals

The NIH Madrigal Singers will present a program of Christmas music and madrigals in Masur Auditorium, Bldg. 10, on Monday, Dec. 19 at 12 noon. Everyone is welcome. □

Clinical Center Gallery Listings

Through Jan. 17:

- Gallery I — Michele Tremaine
- Gallery II — Christine Doyle
Oils
- Gallery III — Elizabeth Burger
Sculpture
- Gallery V — NIH Juried Show
- Lipsett — May H. Lesser
Color Etchings

For more information, contact Gallery Office, 496-8113. □



Gladys Atkinson, who specializes in small and disadvantaged business utilization in the Division of Procurement, has received a PHS Departmental Award for outstanding accomplishments in procurement and the contributions she has made toward maintaining the "excellent reputation in acquisition that HHS enjoys throughout the government." Her efforts were recognized at the HHS Departmental Conference on Acquisition held recently at the Wilbur J. Cohen Building in downtown Washington.

Healthy Men Needed

Healthy men ages 18 to 30 are needed for NIMH study of brain activity. Must be right-handed, native English speakers, with no history of childhood learning or behavioral problems. Interviews and testing, Mon.–Fri., 8 a.m. to 4 p.m. Need 2 weekdays free. Volunteers will be compensated. Call Ashley or Mary, 496-9131. □

MARYLAND ACADEMY OF SCIENCES

announces

Nominations are currently being accepted for

THE OUTSTANDING YOUNG SCIENTIST and THE OUTSTANDING YOUNG ENGINEER OF MARYLAND AWARDS

These awards recognize extraordinary contributions made by young scientists and engineers who live or work in Maryland.

**EACH RECIPIENT WILL RECEIVE THE
ALLAN C. DAVIS MEDAL
AND A CASH AWARD OF \$2,500.**

For nomination information, rules and applications, call the Maryland Academy of Sciences at (301) 685-2370, extension 358.

Nomination and required letters of recommendation must be postmarked by January 31, 1989.