Hallett KO’s Kassirer in 3rd Round

Grand Rounds ‘Bout’ Pits Professor and Physician

Before a standing room only audience in Lipsett Amphitheater, Clinical Center Grand Rounds was transformed into a sort of pedagogic boxing match recently as two physicians squared off for a contest dubbed “The Professor in Action.”

In one corner stood Dr. Jerome Kassirer of Tufts Medical School, armed only with a set of slides and a rather smug silence.

Opposite him stood Dr. Mark Hallett, clinical director of NINDS, whose weapons were a microphone and his many years of expertise in neurology.

Kassirer, appearing in his second “bout” here during CC Grand Rounds, presented his opponent with facts about three different patients he has seen during his career. Hallett’s challenge was to reach a diagnosis once acquainted with the facts in each case.

“Those aren’t oddball cases, but they illustrate things I have learned,” said Kassirer before introducing his first case. “Each one

(See ROUNDS, Page 2)

Kudos Pour In
Rasband Gives NIH Good ‘Image’

By Carla Garnett

Accolades, written in letters and various newspaper clippings packed in bulging filefolders, hail daily from as close by as next door and as far away as Japan and Australia. Some, written in few words, simply ask for Image, while others, more intrigued, want Image explained to them. What is Image?

Image is a Macintosh II computer graphics program developed by NIMH computer systems analyst Wayne Rasband. In the year or so since its conception, the program has generated interest from every corner of the computer industry—users, retailers as well as manufacturers.

In a memo to another staff member, an Image user at the University of California’s Lawrence Livermore National Laboratory explains the program:

“Image is a program for . . . acquiring, enhancing, analyzing, editing, animating and pseudocoloring gray-scale or color images.”

Developed originally to aid medical researchers, Image processes x-rays, autoradiographs, CAT and PET scans, other diagnostic tools and even Polaroid photographs.

The program digitizes these images and displays them on a computer screen. The user

(See RASBAND, Page 6)

Patent Policy Defines NIH-Industry Research Ties

By Leslie Fink

The NIH Patent Policy Board has released the new group’s first formal policy statement, providing a framework for expanding efforts to move the fruits of NIH research out of campus laboratories and into the hands of the consumer. The document safeguards the NIH research mission while recognizing that technology transfer is “a responsibility of each laboratory science and engineering professional.”

The statement “sets the stage” for research alliances between NIH and industry scientists, according to Dr. Philip Chen, NIH associate director for intramural affairs and chairman of the Patent Policy Board. Earlier prototype statements outlining joint agreements weren’t suited to the NIH research environment, Chen says. “Now we have developed our own philosophy of who we are as an agency and, based on our biomedical research mission, how we look at these agreements.”

In 1986, Congress passed the Federal Technology Transfer Act (FTTA) out of concern that beneficial technologies developed by government researchers rarely make it to the marketplace where citizens can buy and use them. At that time, Congress noted that less than 5 percent of government patents were ever licensed to companies for commercial development, according to attorney Reid Adler, director of the NIH’s Office of Invention Development. “And what did get licensed,” he says, “could likely have been developed jointly with a company and commercialized at an earlier stage.” The FTTA, according to Adler, is a move by government to “shift results from this very wonderful and expensive research institution more quickly into the marketplace where people can have access to them.”

A key aspect of the FTTA encourages federal scientists to apply for patents on new and useful technologies or “inventions” they develop in their laboratories. Lawyers call patents “intellectual property,” which lays legal claim to original thought processes that result in a useful invention. According to the new policy statement, “Congress and the President have chosen to utilize the patent system as the primary mechanism for transferring Government inventions to the private sector.”

Under the new law and NIH policy, filing patent applications is an “important component” of a scientist’s research effort. Patents may be issued on inventions developed by intramural researchers working alone or in

(See PATENTS, Page 4)
taught me something extraordinarily interesting and important.

"Incidentally, this contest isn't me versus Hallett. It's Hallett on his own," he said ominously.

The first case involved a 36-year-old clerk with weakness in his arms and legs. Shown a series of slides divulging facts acquired chronologically, Hallett patiently reviewed the relevance and implication of each one, thinking aloud into the microphone.

After several minutes of patient cogitation, Hallett arrived at a diagnosis of myasthenia gravis in case one. Conceded Kassirer, "That was a spectacular discussion of the case."

The second mystery case involved a 27-year-old Chinese man with weakness in his arms and legs for the past half day. Hallett, emphasizing the importance of considering alternatives to the "obviously," quickly—and accurately—indicted hyperthyroidism as the cause of the man's complaint.

The last case was a 52-year-old Bostonian with hemiparesis (half paralyzed) and a history of heavy drinking and smoking. Regarding the latter credentials, Hallett, a Harvard-trained physician, quipped, "This is relatively common in Boston." So quickly did he pinpoint a brain tumor as the source of the man's problems that Kassirer declared, "I think you know who to go to if you have a neurologic problem."

The exercise in thinking on one's feet is meant to illustrate the thought processes physicians use in treating patients, Kassirer said. Members of the audience were invited to contribute to the discussion, and several came to Hallett's aid when he called upon them.

Those interested in attending the next edition of the Professor in Action should consult the CC Grand Rounds calendar, available by calling 496-2563.—Rich McManus

FAES Announces Concert Schedule

The Foundation for Advanced Education in the Sciences will present eight concerts in its 1989-90 Chamber Music Series.

The concert dates are: Oct. 15, Auryn String Quartet; Oct. 29, Jean Louis Steuerman, piano; Nov. 12, Trio d'Archi Di Roma; Dec. 17, Beaux-Arts Trio; Jan. 21, 1990, Cantabile; Feb. 11, Bartok String Quartet; Feb. 25, Andras Schiff, piano; Mar. 11, Uto Ughi, violin.

The concerts will be held on Sundays at 4 p.m. in Masur Auditorium, Bldg. 10. For further information, call 496-7976. —

Powerful Storm Rips County, Damages Campus

The 4:30 p.m. thunderstorm that ravaged northwest Washington and southern Montgomery County June 14 bringing winds measured at 70 miles an hour, dumping torrential rains on the metropolitan area and jamming traffic during the evening rush, did not leave NIH unscathed.

Minutes after the 40-minute storm passed, NIH police and emergency response crews were dispatched to trouble areas, most of which involved downed tree limbs, minor damage to a few cars and traffic redirection.

At 6 p.m. NIH police had blocked Center Dr. between the Clinical Center and Bldg. 31 where a fallen tree lay blocking westbound traffic.

Perhaps the most significant and lasting damage to the Bethesda campus occurred in Bldg. 37 where an eight-story white oak tree was split in half, its top crashing into a fifth floor window of the building’s northwest corridor. Although at least one employee was in the corridor at the time, no one was hurt.

Tom Cook, chief of the NIH Grounds Maintenance and Landscaping Branch, summarized the damage: "Aside from the Bldg. 37 oak tree, four other fairly large trees were knocked over, the trunks of five smaller trees were broken and the rest was just brush."

According to Cook, the area along Cedar Ln. between Old Georgetown Rd. and West Dr., called Cedar Lane Woods, and the large, hilly tract of land that overlooks the Medical Center Metro stop, were two of the campus' hardest hit areas.

"Any area that was fairly open—with lots of trees but no buildings—was hit pretty hard," he said. "We've still got quite a lot of debris to clean up. It (the storm) was a little worse than the real heavy, wet snowstorm we got a few years ago."

A day after the storm, the Westwood Bldg. was still without electricity causing NIH officials to shut down the facility. In terms of damage to electrical distribution and numbers of customers affected, Pepco reported the recent storm as the worst in its 93-year history. An estimated 120,000 to 150,000 customers lost power as a result of the storm.

Approximately 85,000 households and businesses remained powerless for more than 24 hours after the storm, which caused many schools in Bethesda, Chevy Chase, Takoma Park and the District to close.—Carla Garnett

Gusty winds and torrential rains from a recent thunderstorm gave many campus trees a surprise and extensive pruning. Charlene French (c), an NHLBI employee in Bldg. 31, found the tree limb at right on the hood of her car just after the storm. Her car, which was parked on an NIH lot at the corner of Cedar Ln. and Rockville Pk., was one of a few on the Bethesda campus that sustained minor damage.
Scientists Explore Mechanism for Resetting Biological Clock

Scientists supported by the National Institute on Aging have found that carefully timed exposure to bright lights might prove a quick and effective treatment for certain sleep disorders.

In the current issue of Science, Dr. Charles Czeisler, Dr. Richard Kronauer and their colleagues at Brigham and Women's Hospital and Harvard University report that the body's internal clock is more sensitive to light than previously thought and can be "set" by scheduled exposure to light over a relatively short period of time.

Located in the brain's hypothalamus, this internal clock, or circadian pacemaker, controls when we sleep and when we wake, as well as a variety of other bodily activities that influence the way we think, feel and function. Each day, the pacemaker—which runs on a cycle of about 25 hours—is reset to fit the 24-hour cycle of the calendar day. Czeisler and his colleagues have found that light may be the single most important factor in resetting the clock and that the timing of light exposure determines the extent and direction of the change.

As part of their research, the investigators conducted a total of 45 trials in 14 healthy young men. For an average 8-day trial, each subject lived in a laboratory environment devoid of all external time cues. For the first 2 days of the trial, the subjects were kept awake while the investigators performed tests of body temperature, kidney function, alertness and performance to determine the normal setting of their pacemakers. They then experienced 3 days of alternating light (16 hours) and darkness (8 hours). For 5 hours during each light cycle the volunteers sat facing a bank of specially designed fluorescent lamps with an intensity comparable to sunlight just after dawn.

As a result, the investigators found that the human circadian pacemaker can be reset to any desired phase by scheduled exposure to light for 2 to 3 days. More importantly, they found that the same exposure at different times can have significantly different effects. For example, exposure at one time in the cycle resets the clock to an earlier hour, while exposure at a different time resets the clock to a later hour. Exposure at certain times causes very little effect. As part of his work on this project, Kronauer has developed a mathematical model to predict the body's response to any light exposure.

It has been known for some time that the internal clocks of animals and lower organisms are set by daily cycles of light and darkness. Scientists have long felt that in humans, social contacts and other environmental cues play a more significant role than light-dark cycles.

In 1986, Czeisler and his colleagues reported the first evidence that daily exposure to sunlight might be the key to resetting the biological clock. As part of an experiment designed to adjust slight abnormalities in circadian function, the investigators found a dramatic light-induced shift in the biological clock of a 66-year-old woman who was having difficulties with her sleep.

The recent findings indicate that a schedule of alternating light and darkness can be designed so that a person can be alert whenever (s)he needs to be. This research has broad implications for people suffering from jet-lag—some of whom require more than a week to adjust to a new schedule—for those who do rotating-shift work, and for those who suffer from insomnia.

They also have implications for older people. According to Czeisler, "The circadian pacemaker gradually speeds up as a person ages. Over time this could lead to early morning awakenings and other sleep complaints reported by some older people."

New Hope Highlighted at International AIDS Conference

More than 200 NIH researchers attended the Fifth International Conference on AIDS in Montreal June 4–9 where many presentations reflected a new, more hopeful theme that AIDS is now moving toward being a chronic but manageable disease.

Dr. Anthony Fauci, director of NIAID and NIH associate director for AIDS research and Dr. Sam Broder, director of NCI, who both chaired important sessions, were among the more than 130 NIH scientists who had either presentations, posters or chaired sessions.

The conference is the largest ever held on AIDS and drew more than 11,000 physicians, scientists, health care workers and pharmaceutical company officials along with leaders of organizations representing persons with AIDS and gays.

Much of the basic research on AIDS is being conducted through NIH intramural and extramural programs. The World Health Organization estimates that by the year 2000, 15 to 20 million people worldwide will be infected with HIV, the AIDS virus.

Rapid advances in understanding the unique complexity of HIV, including key genes and proteins, however, led many of the Montreal experts to say that controlling AIDS, and the opportunistic diseases characteristic of AIDS, can occur in the foreseeable future.

About six vaccines are in some stage of testing and there are more than 20 anti-HIV drugs being tested. Other compounds under development are targeted toward opportunistic infections. Some drugs are in combination trials that may lead to multidrug therapies much like those that have been effective controlling certain cancers. In the United States, about 7,000 AIDS patients have been enrolled so far in NIH protocols.

Meanwhile many of the scientific presentations in Montreal focused on current advancements in care and management of persons with the AIDS virus that are already adding months or years to the average life expectancy and improving the quality of life.

These treatments include aerosolized pentamidine as a prophylactic for pneumocystis carinii pneumonia, which has been responsible for nearly 70 percent of AIDS-related fatalities and AZT, which inhibits replication of HIV among those who can tolerate the drug.

The evidence presented at Montreal of the advantages of early medical intervention may increase the demand for medical care facilities and drugs.

Other seminars at the conference dealt with public health issues, funding, prevention and education, along with social issues such as discrimination against persons with AIDS.

Because the conference had become so large there was discussion of whether future conferences should be more focused on biomedical research with a separate conference on public health and social issues. The Sixth International Conference on AIDS will be held in San Francisco, June 20–24, 1990.
PATENTS
(Continued from Page 1)

technology transfer collaborations with industry scientists.

The 13-member Patent Policy Board was established in 1987 to evaluate and recommend policies regarding the patenting of inventions by NIH researchers. The board reviews the terms of [model] research agreements between NIH and industry researchers, decides how royalties will be distributed, and how a scientist may use royalty dollars brought in by his or her patent. The board also sponsors training sessions to familiarize scientists with the details of technology transfer.

The increasing use of DNA-splicing enzymes that allow scientists to create new combinations of genetic material, endowed with novel characteristics and functions, has redefined the term "invention" for patenting purposes. Now many scientists working in biomedical research laboratories use gene-splicing techniques in their day-to-day investigations; some of these processes, and molecules derived from them, may be patentable. Because of recent court decisions, molecular probes, gene regulation sequences, transgenic plants and animals, vaccines, gene vectors, and monoclonal antibodies are all patentable if they pass certain legal tests. So are many other molecules and processes derived from laboratory work.

Last year, the NIH filed more than 150 patent applications with the U.S. Patent and Trademark Office and expects to exceed 200 this year.

"The biggest problem for people at NIH who are novice at the process of technology transfer is knowing when they have an invention to file a patent for," says NIAID's Dr. John Gallin, who is a member of the NIH Patent Policy Board. "We're developing vaccines and therapeutics, products that have an obvious use. But other products might not be so obvious."

As director of NIAID's intramural research program, Gallin oversees a group of scientists who rank second among NIH institutes in the number of patents awarded to an intramural program. Because of NIAID's interest in immunology and infectious diseases, patentable products include candidate vaccines for hepatitis, malaria, infant diarrhea, Lyme disease, sexually transmitted diseases, and AIDS, as well as molecules that may be used to treat AIDS and other immune system disorders.

Scientists who suspect their work has resulted in a patentable invention, says Gallin, should consult their scientific directors to determine whether a patent application should be filed. If so, the scientist would then submit an invention report to the NIH Patent Branch, in the Office of the General Counsel.

A good time to file a patent application, according to Gallin, is at the same time any scientific manuscript or conference abstract describing the work is submitted for publication. An application for a U.S. patent may still be filed up to one year after publication of the invention. But any rights to foreign patents are lost unless a U.S. patent application is filed on the invention before publication or other public disclosure of the work. A patent, whether from a joint agreement with industry, or from a single intramural scientist, is only one step in transforming a laboratory result into a marketable product. While a patent gives a scientist a period of exclusive claim to his or her invention, it does not give the scientist the right to make, use, or sell the invention. The Food and Drug Administration, for example, regulates the sale of drugs even if they are patented.

The reason for a patent's period of exclusivity, the statement says, "is to encourage industry to invest the resources necessary to bring an invention from the discovery stage through subsequent development, clinical trials, regulatory approval, and ultimately into commercial production." So through commercialization licenses, NIH patent holders agree to share their exclusive rights with private companies who will move the product through these steps.

In addition to patent policy, the 18-point statement lays down guidelines for research agreements between NIH scientists and outside collaborators. With the spawning of hundreds of biotechnology companies over the past decade and a half, biomedical discoveries now have a commercial outlet they've never had before. "As biotechnology as an industry has risen," Philip Chen says, "links between companies and the NIH have accelerated."

These agreements, called Cooperative Research and Development Agreements (CRADAs), tap industry expertise in recognizing and steering a basic research product toward commercialization. NIH scientists may enter into CRADAs with industry collaborators who will "make a significant intellectual contribution to the research project" or who will contribute essential materials and technical resources.

Patents on inventions that arise from work performed jointly under a CRADA are coowned by the NIH and the collaborating company. Generally, the company involved in the work will also be granted a commercialization license to develop the invention into a marketable product.

"I think it's also very exciting that even on one disease, AIDS for example, there are several companies working with the same lab," says Reid Adler. "Industry is coming in on the ground floor of the research and will be able to transform the results into a useful product more quickly than if the lab had simply filed a patent application several years down the road."

One important goal of the policy statement, says Adler, is to ensure that government scientists continue the free pursuit of biomedical research while recognizing which research projects may lend themselves to patents and CRADAs. "The policy statement attempts to strike a balance between technology transfer and our freedom to do the research we need to do," he says. "We won't ignore our agency mission, which is basic biomedical research, simply to play the technology transfer game."

"I don't think technology transfer is going to change the direction of NIAID research," says John Gallin. "It's making people aware that their research is potentially valuable, and it's fostering much more collaboration with industry. That will result in a more expeditious transfer of laboratory observations into useful products. I think that's good."
NIAID Creates Sexually Transmitted Diseases Branch

Sexually transmitted diseases (STDs) are a growing, major public health problem. More than 20 infectious agents are transmitted by sexual means and the STDs they cause are associated with a wide variety of acute and chronic health problems. The economic impact alone is estimated to total billions of dollars annually in the United States.

To better meet the needs of the research community in combating this problem, NIAID has created an STD branch and named Dr. Judith Wasserheit as its chief. Although NIAID has long supported STD research, individual research grants and contracts had been distributed throughout the institute.

“We want to provide a visible and responsive administrative focus for the STD research community at large and others interested in advancing STD research,” said Dr. Anthony S. Fauci, institute director.

Research within the new STD branch is directed at prevention and control of STDs and their complications, which include infertility, ectopic (tubal) pregnancy, cervical cancer, fetal loss and prematurity. Chlamydial infections, gonorrhea, trichomoniasis, syphilis, chancroid, pelvic inflammatory disease (PID), genital herpes and genital warts are among the diseases under the domain of the new branch.

Research on AIDS, hepatitis B, and cytomegalovirus infection is supported in other NIAID program areas.

“One of the few positive aspects of the AIDS epidemic has been to focus attention on STDs not only as important cofactors in transmission of the human immunodeficiency virus, but also as common diseases that result in devastating, long-term sequelae, particularly for women and infants,” said Wasserheit. “We now have a unique opportunity to combine recent advances in biomedical and epidemiologic research methods with innovative approaches to behavioral research in order to develop insights and interventions for combating STDs.”

Before coming to NIAID, Wasserheit was an assistant professor of medicine in the division of infectious diseases at Johns Hopkins University School of Medicine. She also served as medical director of the Druid STD Clinic and assistant chief of STD Clinical Services for the Baltimore City health department.

Wasserheit received her B.A. in biochemistry and Slavic languages from Princeton University, and her M.D. from Harvard Medical School. She completed her house staff training at Columbia Presbyterian Medical Center in New York and the Emory University Hospitals in Atlanta, and her infectious diseases fellowship at the University of Washington in Seattle. She subsequently spent 2 years at the International Centre for Diarrhoeal Disease Research in Bangladesh conducting a population-based study of genital tract infections among rural women. Wasserheit is particularly interested in the impact of genital tract infections on women’s reproductive health.—Sandy Hecker

Rall Receives Medal from Finland

Dr. David P. Rall, director of the National Institute of Environmental Health Sciences, received the Distinguished Service Medal from the Institute of Occupational Health, Helsinki, an agency of the Finnish government. The medal was conferred by director general of the Finnish Institute, Dr. Jorma Rantanen, at a banquet concluding an international scientific meeting on risk assessment of complex mixtures held recently in Espoo, Finland.

Rantanen also presented Rall with a certificate stating that the award was “in recognition of excellent work in the field of occupational health and safety and especially for (his) contribution to the development of occupational health in Finland.” NIEHS and the Finnish Institute of Occupational Health have collaborated in the area of environmental and occupational health under a formal bilateral agreement since 1982.

Rall joined NIEHS as director in 1971. During his service, the institute in Research Triangle Park, N.C., has grown from a fledgling facility and organization with several hundred employees to a world center for toxicological research employing 900, which takes a leading role in U.S. international agreements in environmental research with many other nations and within the World Health Organization.

“In addition to receiving the Distinguished Service Medal, Rall delivered one of the keynote lectures titled “Carcinogens in Our Environment.”

“It is clear that it is difficult to categorize and characterize individual agents as carcinogens. As we enter the more complex arena of multiple exposures and combination toxicity, we urgently need better methods and a better conceptual framework,” he concluded.

Rall has received many distinctions and honors, including membership in the Institute of Medicine of the National Academy of Sciences; recipient of the Alumni Merit Award from Northwestern University; and recipient of the Arnold J. Lehman Award from the Society of Toxicology.—Thomas Hawkins
The Record
June 27, 1989

RASBAND

(Continued from Page 1)

Image, a computer program developed for the Macintosh II by NIMH's Wayne Rasband, enables users to analyze x-rays, autoradiographs, CAT and PET scans and other diagnostic materials on computer screen. By using a combination of the tools shown at left, a researcher can draw lines to measure areas or add pseudocolor to improve contrast. Image automatically displays measurement results in the legend at right.

can then manipulate the onscreen image in a number of ways.

For instance, a PET scan showing the presence of a brain tumor is converted by Image for the video screen. A researcher who wants to know the size of the tumor can trace the mass, highlighting the tumor.

Automatically, Image computes the size of the highlighted area and displays the measurement in seconds.

Using one of Image's many options, the researchers can also add pseudocolor to show contrast between the tumor and surrounding areas or add animation to simulate motion. Filtering functions sharpen the PET scan image, smoothing rough edges or blocking out extraneous "noise" in the picture.

Most benefits of Image become clear the moment the program is seen in action. However, the greatest unseen asset of the program, at least as far as non-NIH'ers are concerned, is probably its availability and cost-efficiency. Image is less than cheap; it's free.

Because Rasband created Image as a NIMH employee, the program has no copyright protection and essentially belongs to the public. Similar graphics programs with comparable functions cost about $2,000 for each copy. Image is available without cost by contacting Rasband or through various computer networks worldwide.

Much of the world has already recognized the value of Image. Rasband's file contains hundreds of notes, handwritten as well as typed, from all over the United States—Nevada, Arkansas, Minnesota and New Mexico, as well as overseas—Canada, Germany, Denmark and Australia.

"Ninety-five percent of them are from the U.S.," said Rasband, a 20-year NIMH veteran, "although (Image) has seemed to spark more interest in Germany for some reason."

One satisfied customer from the University of Cologne in Germany writes to Rasband:

"You created an excellent program to analyze digitized scans, x-rays or simple color pictures. As a surgeon, I would appreciate a program, which would enable me to followup CT-scans of bones ... Your program could be an ideal solution."

Another kudo from an orthopedic rehabilitation hospital in Canada reads:

"(Image) has accelerated our work related to medical image processing ... suffice it to say that we are very keen to keep in touch and would be pleased to provide more details on how we are using Image."

One enthusiastic Bostonian used Image to convince the rest of his department to buy Macintosh computers. He writes to Rasband, "You can't believe what a commotion your software is making with everyone I demo it to. People are just blown away!!! In the face of IBM uniformity (in five other centers in his company) ... Image was the key sales pitch. The performance and interface is fantastic! It stands virtually unchallenged from the commercial sector and is available at no cost, it is without doubt my favorite application."

Rasband developed Image for his favorite computer—the Mac II.

"It's easy to use," says Rasband. "It behaves consistently and there's a lot of carryover from program to program. You don't have to start from scratch."

Before Image and the Mac II-video camera system, researchers studying the brain used images that were acquired from a rotating drum film scanner and analyzed on minicomputers. Several problems made that system costly and tedious.

"The minicomputers and drum scanner were expensive to maintain," noted Rasband, who developed the first edition of the Mac II program in a few weeks. Within the last 18 months, subsequent editions of Image have emerged, each packed with more functions and fewer "bugs."

"The old system was unreliable. And although Image is not yet finished, the Mac II system that uses it is much less expensive," he said.

Rasband has written other programs for use on the Mac including PAM, which stores and analyzes activity data acquired by patient activity monitors.

The activity monitors were developed by engineers in Rasband's Research Services Branch in 1975 to study abnormal behavior cycles in manic-depressive illness. Rasband converted the minicomputer-based software for PAM to the Mac in about 6 months.

MacMeasure, a program similar to Image that is used for analyzing photographs using a digitizing tablet, took Rasband 3 or 4 months to create.

Rasband continues to improve Image. The most recent feature he is developing will allow users to create computer-generated legends for defined areas.

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Wayne Rasband

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"Image does basically everything a graphics department could do," he said. "It prepares slides, materials for presentations ... there are still things to add, though."
Dr. Richard Klausner, chief of NICHD's Cell Biology and Metabolism Branch, delivered the presidential lecture to the Endocrine Society at its annual meeting June 21 in Seattle. The Endocrine Society honored Klausner for his fundamental contributions to the understanding of RNA regulatory elements.

The regulatory elements that Klausner and his colleagues have discovered are of crucial importance to the cell because they control intracellular iron levels. Iron has a central role to play in cellular metabolism and proliferation; with either too much or too little iron, cells can't survive and divide.

Two proteins in the body are of particular importance in keeping iron levels constant: to take iron in from the circulation, the cell surface has a special receptor, called the transferrin receptor (TfR); inside the cell there is an iron "sponge" called ferritin, to remove iron if too much accumulates. Cells balance iron levels by regulating the production of these two proteins. Accordingly, if the iron level in a cell falls and more needs to be taken in, TfR production is kept high and ferritin level in a cell falls and more needs to be taken up sufficiently to be able to drape itself over the IRE's; when iron levels are high, the protein becomes too compact to fit over the IRE.

One question this research has also been able to solve is how iron levels can have opposite effects on TfR and ferritin production. Although the stem-loop structures of both TfR and ferritin IRE's have similar nucleotide sequences, they were found to be located at opposite ends of their respective messenger RNA molecules—near the beginning of ferritin messenger RNA and near the end of TfR messenger RNA. When the ferritin IRE is occupied by the iron sensing protein, translation of messenger RNA into ferritin is blocked. With less ferritin present, more iron becomes available to the cell. When the IRE of TfR messenger RNA is occupied, RNA degrading enzymes cannot bind to the messenger RNA and cleave it, keeping it available to the cell for production of TfR.

Although still early in his career, Klausner has an international reputation as a pioneer in several fields of biology and medicine, in addition to iron metabolism. Because of his versatility, he has been able to use the insights gained in one field of endeavor to illuminate those in another. His innovative research in receptor-mediated endocytosis and the structure, assembly and mode of action of the T cell antigen receptor is widely regarded as outstanding. He is the recipient of a number of other awards and honors, including the Young Investigator Award of the American Federation of Clinical Research and the Meritorious Service Award of the U.S. Public Health Service. —Birgit An der Lan

**Fogarty Adds Ex-Officio Members**

Three ex-officio members have been appointed to the Fogarty International Center advisory board.

They are Dr. Lawrence E. Shulman, director of NIAMS; Dr. Jay Moskowitz, NIH associate director for science policy and legislation; and Dr. Nyle Brady, senior assistant administrator, Bureau for Science and Technology of the U.S. Agency for International Development.

Shulman replaces Dr. John Decker, director of the Clinical Center, on the board.

Moskowitz represents the Office of the Director, NIH. Brady represents AID, with which the Fogarty center has extensive liaison in international health matters.

**Dugger Appointed NIH Federal Women's Program Manager**

Linda S. Dugger was recently appointed Federal Women's Program manager in NIH's Division of Equal Opportunity.

Dugger previously worked as equal employment opportunity officer for 7 years with the U.S. Army in West Germany. Prior to her work in equal opportunity she was an educator in Ohio public schools and at the University of Toledo in Ohio.

In 1973, Dugger received her B.Ed. from the University of Toledo. She received her M.Ed. in educational administration from the same university in 1974.

She has been active as a community volunteer by serving as an American Red Cross instructor in first aid and in preparation for parenthood, a Girl Scouts leader, and a team member for rape crisis intervention. She has developed or sponsored two Toastmasters clubs in West Germany and has achieved the status of Competent Toastmaster.

Dugger's goals as Federal Women's Program manager for NIH include strengthening NIH networks for women and increasing the NIH community's awareness of women's issues. She sees her primary role as facilitator and views the program as a means of enabling women to develop and achieve their career goals.

Inquiries regarding the NIH Federal Women's Program should be directed to Dugger, 496-2112.
Straus Explains Fatigue Syndrome to Legislators and Their Staffs

By Ellyn J. Pollack

Imagine being so exhausted from a simple daily task that you have to go back to bed. While many people occasionally complain that they are tired and do not want to go back to work for a couple of months, some people are always so exhausted that even the simplest task becomes a hurdle to overcome.

Chronic fatigue syndrome (CFS) is a debilitating disorder that impairs an individual's ability to participate in normal daily activities, said Dr. Stephen Straus, chief of the NIAID medical virology section, addressing 75 people on Capitol Hill during a repeat of his 1988 Medicine for the Layman lecture. Patients with CFS also have difficulty concentrating or remembering what they have to do. They are easily distracted and have cognitive problems.

NIH deputy director Dr. William Raub introduced Straus, whose lecture was the first in a series of Medicine for the Layman lectures to be delivered on Capitol Hill.

The NIH Legislative Affairs Office asked the Office of Clinical Center Communications to reproduce its popular Medicine for the Layman lectures on Capitol Hill in an effort to inform Congress about research at NIH. Rep. John Porter of Illinois sponsored the first lecture, providing the room and publicity, the NIH Medical Arts and Photography Branch supplied equipment for the slide presentation, and NIAID provided donuts, coffee and juice for the audience.

The second lecture, given by Dr. Marilyn Gaston, deputy chief of the NHLBI Sickle Cell Disease Branch, will be sponsored by Rep. Louis Stokes of Ohio. Gaston will discuss sickle cell anemia. The lecture is tentatively scheduled for July 30.

CFS is not a single disease, Straus reported, but probably a mixture of various factors that lead people to be chronically fatigued. Patients with CFS are always tired to some degree, and easily exhausted. They often experience recurring dull headaches, joint and muscle aches, a sense of feverishness and chills, tender lymph glands, difficulty in concentrating on assigned tasks and depression.

Two-thirds of those diagnosed with CFS are women who were previously active; the majority are middle-class and Caucasian. Many patients relate the onset of their fatigue to a specific infection, usually a respiratory or gastrointestinal infection such as influenza, bronchitis, a sore throat, a cold, diarrhea or abdominal cramps. These infections usually are not severe in the beginning and only last a few days. But people with CFS find themselves waiting day after day to get back on their feet, Straus explained. Similar problems that last for only a few days or weeks are probably common, but when symptoms persist for more than 6 months, they may indicate chronic fatigue syndrome. However, numerous other causes of fatigue first need to be excluded.

CFS, in addition to beginning with acute infections, often begins at a period of great stress or at some special event in the person's life such as divorce, career changes, moving or death in the family.

People with CFS often have allergies, Straus said, which suggests the immune constitution of these patients may be abnormal before the fatigue begins. Other signs of immune problems in CFS patients also have been reported. For example, investigators found a slight reduction in the ability of blood cells in CFS patients to produce interleukin-2 and gamma interferon, important chemicals in mediating our immune responses to cancers and infectious agents.

Researchers have found that many patients with CFS also have clinical depression. The relationship with depression often is not understood, but there are similarities between the two disorders. Patients who are depressed have low natural killer cell activity, abnormalities with lymphokine and interferon production, and occasionally have abnormalities of antibody production to certain viruses, all features of CFS.

Straus said doctors can offer CFS patients symptomatic therapies such as anti-inflammatory medications for headaches, muscle aches and joint aches; aspirin or Tylenol for chills and feverishness; adjustment in daily habits or dietary habits for difficulty with sleeping; and antidepressants when appropriate; and guidance for coping.

Use of Smokeless Tobacco Highest Among Young Men

Scientific data from three recent surveys show that use of smokeless tobacco among teenage and young adult men in the United States is a significant and growing problem. Use of smokeless tobacco is highest in the South and lowest in the Northeast part of the country. States with exceptionally high rates of smokeless tobacco use among men include West Virginia, Mississippi, Wyoming, Arkansas, Montana, and Kentucky.

Overall, it is estimated that 2.2 percent of white men in the U.S. use snuff and 4.3 percent use chewing tobacco. Black and Hispanic men are similar in their reported use of snuff, with both groups reporting a much lower rate compared to white men. With respect to chewing tobacco, black men ranked second to whites, and Hispanics ranked third.

The national rate of smokeless tobacco use among women is less than 1 percent, compared to 5.5 percent among men.

Almost half of men age 18 and older who use smokeless tobacco are daily users. Some substitute smokeless tobacco for cigarettes, but most tend to use both forms of tobacco. Rates of smokeless tobacco use are highest among white males 12 to 25 years of age living in nonmetropolitan areas.

These data and 13 other studies on smokeless tobacco use are published in the National Cancer Institute's new monograph, Smokeless Tobacco Use in the United States. The monograph also explores the current problem of smokeless tobacco use by youths such as predictors of onset of use, factors that influence use, patterns developed, and the relationship of smokeless tobacco use to other substance use. The cancer risk associated with smokeless tobacco and future directions of research are also discussed.
NIDR Studies Oral Manifestations of AIDS

On May 30 the National Institute of Dental Research and its cosponsors of a new study on the oral effects of the human immunodeficiency virus (HIV), held an open house at the study's research site. The clinic is located in a newly renovated wing of the old hospital at Walter Reed Army Medical Center. The event was held to thank the many people who worked toward opening the clinic and launching the study.

The study, "The Natural History of Oral Manifestations of HIV Infection in a United States Military Population," is part of a parent project being conducted by the Walter Reed Army Institute of Research (WRAIR) on the natural history of HIV infection. The U.S. Army Dental Activity at Walter Reed and the U.S. Army Institute of Dental Research also are supporting the project. The Henry M. Jackson Foundation, a nonprofit organization that supports military medicine, is handling administrative management of the study.

"I'm pleased to see this facility become a reality," said Dr. Harald Loe, NIDR director. He credited the efforts of the Army Dental Corps and the other collaborators for the successful development of the facility. Maj. Gen. Bill Lefler, chief of the U.S. Army Dental Corps, said the project was a tremendous milestone in the fight against AIDS.

The overall objective of the study is to document the prevalence and incidence of oral conditions that appear during various stages of HIV infection and define risk factors associated with these conditions.

"This is a unique study for two reasons," said Dr. Philip Swango, the study's principal investigator. "First, the volunteers already are enrolled in the larger WRAIR study so we will be able to evaluate the oral findings within the larger medical context. Second, many of the individuals are in the earliest stages of infection and are asymptomatic."

Swango, a PHS dentist in NIDR's epidemiology and oral disease prevention program, explained that active duty military personnel are required to be tested on a routine basis—ensuring that all new cases are caught early.

The research initially will follow four directions. The first goal of the study is to characterize the range and severity of HIV-associated oral conditions as they relate to the progression of HIV infection. Since oral conditions occurring early in the course of infection might be predictors of the development of AIDS, verification of this predictive value would allow early diagnosis and permit prompt treatments as they become available.

A second focus of the study is oral candidiasis, a yeast infection in the mouth. It already is considered a reliable predictive marker for the development of AIDS in HIV-infected individuals. Both clinical and microbiological findings will be analyzed in relation to systemic disease progression.

Also to be studied is an aggressive and painful form of periodontal disease that leads to rapid bone loss—one of the more debilitating oral consequences of HIV. This disease is characterized by spontaneous bleeding, ulceration and pain. Dental scientists hope to learn more about this type of periodontal disease and its relationship to an atypical form of gingivitis thought to be one of the earliest signs of HIV infection.

Finally, researchers will explore compositional changes in saliva in relation to the stage of infection and to the risk of disease progression.

Study participants are Army personnel and their family members participating in the umbrella study being conducted by WRAIR.

There will be approximately 1,000 volunteers in the oral manifestations study.

Fantastic' Night with Orioles

Special Love, Inc. and Camp Fantastic invite you to "Fantastic Night with the Baltimore Orioles" on Saturday, July 15 at Memorial Stadium. The evening kicks off with a bullpen party at 5:30, where you'll be treated to hamburgers, hot dogs, beverages and a few surprises. Then watch the Orioles vs. the California Angels from box seats. Cost for the evening is $15 and includes food, beverages and box seat for the game. A portion of the ticket price will benefit Camp Fantastic, a summer camp for kids with cancer. For tickets or more information, contact the R&W Activities Desk in Bldg. 31, 496-4600.

Danford To Direct Nutrition Research Division

Dr. Darla Danford was recently appointed director of the Division of Nutrition Research Coordination (DNRC) in the Office of Disease Prevention, OD. In this capacity, she will also serve as chairperson of the NIH Nutrition Coordinating Committee (NCC).

The DNRC, created in May 1988, coordinates the NIH nutrition research and training activities supported by its institutes, divisions and centers. In addition, the office also serves as nutrition liaison for NIH with the federal agencies, and offers consultation on nutrition issues to the NIH director and the associate director for disease prevention.

"A major component of the division is the
FIC Scholar Kamen Gets Scott Award

Dr. Martin Kamen, a scholar-in-residence at the Fogarty Center, has received the John Scott Award for his discovery and isolation of carbon-14. The award is given to the "most deserving" men and women whose inventions have contributed in some outstanding way to the "comfort, welfare and happiness" of mankind. It is presented by the board of directors of the Philadelphia City Trusts.

In a letter notifying Kamen of the honor, the board cited the wide use of carbon-14 in archeology, geochemistry and medicine as well as its use in the "carbon-dating" method of establishing the age of objects.

The discovery of carbon-14, the long-lived radioisotopes of carbon, came at an early point in Kamen's distinguished scientific career at a University of California lab in Berkeley. Kamen and his collaborator Dr. Samuel Ruben were bombarding targets in the cyclotron developed by Lawrence and Livingston.

"I knew it was there and how to get it, but I didn't know how long it would take," Kamen said in a recent interview. "The longer lived something is, the harder it is to find." The two young scientists made the discovery in February 1940. Kamen described the event in Science in 1963.

Kamen and Ruben then went on to work on different facets of the Manhattan Project. Ruben died tragically in a laboratory accident in 1945.

Kamen has made innumerable original contributions to science; much of what we know today about biochemical mechanisms in metabolism, photosynthesis and many other areas of research stems from his work. His autobiography, Radiant Science, Dark Politics, (Berkeley: University of California Press, 1985), speaks of these accomplishments despite the difficulties that severely interrupted his research during the turmoil generated by Sen. Joseph McCarthy in the 1950's.

As a Fogarty scholar-in-residence at NIH, Kamen is associated with the Laboratory of Biochemistry, NHLBI, and a number of other research laboratories. He has blended research on cytochromes c with a delightful series of lectures in 1988 on the science and music of 19th century scientist T.W. Engelmann. He is now in his second term as scholar.

The John Scott Award honors a pharmacist from Edinburgh, Scotland, who appreciated the accomplishments of Benjamin Franklin and established a fund for Philadelphians entrusted with Franklin's legacy to honor "ingenious men and women who make useful inventions."

Kamen says he will share the $10,000 award with Helena Ruben, Samuel's widow.

Other distinguished John Scott Award honorees include Madame Curie, Thomas Edison, the Wright brothers, Jonas Salk, Glenn Seaborg and Gordon Gould, inventor of the laser.

Kamen's office is in Stone House, Bldg. 16, Rm. 214; phone extension 8733. —Elizabeth Gillette

Seminar Series for Grants Associates and Health Scientist Administrators Starts in September

Each year, the Health Scientist Administrator Development Programs (HSADP) Office in the Office of Extramural Programs organizes a series of seminars in order to complement the working assignments of the GAs (grants associates) and HSA trainees and the working experiences of HSAs. The HSADP Office is accepting applications for its 1990 GA/HSA Seminar Series, scheduled to begin on Friday, Sept. 15. These weekly seminars of 10 months duration are held on Fridays in the Claude Pepper Bldg. (Bldg. 31), generally in the mornings. However, approximately 10 Fridays during this series will be full days.

The seminar series is designed to address a broad spectrum of philosophical, political and policy issues relevant to the administration of federal programs in the support of biomedical and behavioral research; factors affecting extramural programs and their administration; program planning and evaluation; and the legislative/budget process.

HSAs with 1-to-3 years' experience are expected to profit most from and contribute to the series. This does not imply that non-HSAs, including intramural scientists, would not benefit. Those nominees with less than 1 year's NIH extramural experience must have taken the "Fundamentals of NIH Extramural Activities" course to be considered.

Interested individuals should forward a memo stating their interest, as it relates to their current duties, through their immediate supervisor to their BID director, together with a current CV, with emphasis on their present responsibilities. Please be sure to include your current title, BID organizational component and current room, building, and phone number. Each BID director is being asked to forward no more than three nominations with the above noted information and any other supporting documents, no later than Tuesday, July 25, to A. Robert Polcari, director, HSA Development Programs, Claude Pepper Bldg., Rm. 5B32.

These three nominees are in addition to nominees who are in or have recently completed either the newly hired HSA training program or the HSA trainee program. Such trainees are given priority for selection and do not count against the limit of three nominees per BID.

Only a limited number of participants can be accommodated. Selections will be made by Dr. George J. Galasso, NIH associate director for extramural affairs. All nominees whose documents reach the HSADP office by July 25 will be notified of final action approximately in late August.

Participants will receive training credit hours in their official personnel files after completing the series. For further information, contact A. Robert Polcari, director, or Roberta Light, program assistant, HSA Development Programs, 496-1736.
TRAINING TIPS

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

Courses and Programs   Dates

Management and Supervisory 496-6571  
Attitudes: How They Affect Productivity  7/11
Creative Basics for Changing Workplaces  7/12
Working With Personal Differences: MBTI  7/19
Applications for Professional Development  7/18
Practical Approaches to Stress  7/21

Office Operations Training 496-6211  
Introduction to Working at NIH for New Support Staff  7/17
Basic Time and Attendance  7/6
Reducing Stress: Rebuilding Energy  7/12
Delegated Acquisition  7/24
Travel Orders & Vouchers  7/24

Training and Development Services 496-6211  
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.-7:00 p.m.
Friday  8:30 a.m.-4:30 p.m.
Saturday  9:00 a.m.-1:00 p.m.

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Executive Potential Program

The Office of Personnel Management’s Executive Potential Program for high potential mid-level employees is a career enhancement program that is coordinated by the NIH Training Center. It provides training and developmental experience to prepare them for future opportunities as federal managers and executives.

Participants are nominated by their departments as having demonstrated managerial potential. Jim Vennetti, senior program analyst, DCG, was nominated and selected for the 1989 OPM Executive Potential Program. Vennetti is spending 12 months, March 1989 through March 1990, in developmental work assignments, classroom training courses and cluster group participation. His first rotational assignment is serving as the executive assistant for management in the Office of Human Genome Research, OD.

Training is designed around the management excellence framework (MEF) and provides an understanding and working knowledge of, and development in, OPM’s management competency-based model of effective performance for federal managers.

The program will be announced for FY 1990 in September 1989. The NIH Training Center, 496-6371, will have information at that time.

Clinical Center Social Work Chief Stan Kissel Dies

Stanley J. Kissel, Jr., chief of the social work department at the Clinical Center, died May 18 following heart surgery at Walter Reed Army Medical Center.

He joined the Public Health Service in 1962 after completing his master’s degree in social work at St. Louis University. His many assignments included chief social worker at Staten Island PHS Hospital; personnel management specialist of the Commissioned Personnel Operations Division for the health services officer, scientist and veterinarian categories; chief of the social work department at Baltimore PHS Hospital; and chief of the social work staff, Bureau of Medical Services, Division of Hospitals and Clinics, in Hyattsville, Md. In 1980, he joined NIH as chief of the social work department for the CC.

During his career, Kissel served as president of the three Commissioned Officers Association branches, including the D.C. Metropolitan Area Branch in 1981-82. He was general chairman of the 19th and 21st annual meetings of the USPHS Professional Association. As a long-standing member of the American Public Health Association, he served on its governing council from 1986 to 1988 and was editor of the social work section of its newsletter from 1983 to 1989. He also served as editor of the “National Health Line” in the Health and Social Work Journal from 1983 to 1987.

Kissel wrote a number of papers and made many presentations during his career, including “The Identification of Key Results for Clinical Social Work Initiatives in a Medical Setting,” which was presented at the first national health conference of the National Association of Social Workers in Washington, D.C., in 1984. He continued to develop qualitative and quantitative measures of the efficacy of the social work role in health care throughout his career.

Kissel received two PHS Commendation medals (NIH and HRSA) in 1983 and 1980, respectively; a PHS citation in 1981; and the Director’s Award and PHS Plaque, Bureau of Medical Services, in 1979.

Born May 20, 1937, in Johnsonburg, Pa., Kissel is survived by his wife, Vivian; three children, Brian, Cheryl, and Brett; his parents, Kathyn and Stanley J. Kissel, Sr.; and a younger brother, Jerry.
Celebrity Golf Exhibition Benefits Children's Inn

For the past 7 years, the local park commission has allowed television sports reporter Glenn Brenner of WUSA-TV to hold a pro-celebrity golf clinic and exhibition for the benefit of area charities.

This year, Gordon Peterson, anchorman for WUSA and a board member of the Friends of the Children's Inn, persuaded his TV sidekick to earmark all proceeds from the golf clinic—some $10,000—for the Children's Inn at NIH.

On Saturday, June 10, hundreds of area golf enthusiasts collected at Paint Branch Golf Course in College Park to watch such personalities as Sonny Jurgensen, Mark Rypien and Washington Capitals hockey star Mike Ridley play 18 holes of occasionally exemplary golf.

Before the clinic began, Rep. Steny Hoyer (D-Md.), a friend of NIH and a supporter of the inn, greeted guests.

"The Children's Inn at NIH will be a great place for the physical and psychological health of children," he said. "Many of my colleagues in Congress have joined in this incredibly positive effort to create a place where parents can stay with their sick children. The inn is going to keep families together."

Hoyer noted that his hosts Brenner and Peterson each have several children who are healthy, and pointed out that "That's a gift."

Following Hoyer's remarks, Peterson announced that former Speaker of the House of Representatives Tip O'Neill contributed a check for $1,000 to the inn.

Currently under construction on the north side of the NIH campus, the Children's Inn will be a home away from home for up to 36 young NIH patients and their parents. Construction costs of about $3.5 million have been underwritten by Merck & Co. Inc., a pharmaceutical firm. Local developer Alan Kay is overseeing construction of the home.

The golf clinic is only one of many efforts to raise money to endow the inn. A future issue of the Record will provide details of the remarkable community response to the project.

Employed Mothers of Infants

The NICHD seeks employed mothers with a first-born, healthy infant no older than 5 months to participate in a study of social and cognitive development in infancy. Participants must use one of two types of childcare: a housekeeper in the baby's home or a family daycare provider outside of the home. Participants must also participate in a study of social and cognitive development in infancy.

Call for Abstracts for NIH Research Day Posters

The next NIH Research Day will be held on Tuesday, Sept. 26. Symposia on gene expression, developmental biology, oncogenesis, and neurotransmitters, as well as numerous workshops are now being organized. An evening picnic with music by the Bluegrass Express band is also planned.

As in past years, a midday poster session—with 300 presentations—accompanied by box lunches will be a central feature of Research Day. It is expected that many senior and junior scientists will present posters on topics including molecular genetics, cell biology, immunology, virology, neurobiology, receptors and signal transduction, clinical investigations and information processing.

The NIH Research Day committee invites submission of brief abstracts, with titles, authors and institutional affiliations, by all NIH, NIMH, NIAAA and FDA staff from the Bethesda campus. Please send these by July 15 to Dr. Alan N. Schechter, Bldg. 10, Rm. 9N307. Please include full mailing address of the corresponding author.