

## NCI Researchers Gauge Radiation Effects in Mice

Radiation research scientists of the National Cancer Institute have devised a technique for measuring exactly in mice the tumor-damaging effects of irradiation. The procedure gives such predictable results that it can readily be adapted, for example, to study of the ability of drugs to augment the anti-tumor action of irradiation.

Drs. J. Robert Andrews and Roger J. Berry of the Institute's Radiation Branch reported their findings in two papers presented May 15 at the Ninth Annual Meeting of the Radiation Research Society in Washington.

The technique described by Drs. Andrews and Berry provides an exact measurement of the viability of irradiated tumor cells of an experimental mouse leukemia, P-388. The investigators determine how many irradiated tumor cells are needed to achieve 50 percent "takes" on transplantation into susceptible mice.

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## Semi-Automatic Scanning and Plotting Available in New NIH Graph System

A semi-automatic scanning and plotting system has been installed in the Computation and Data Processing Branch, Division of Research Services, and is ready to provide the NIH investigator with records of curve values in the form of punchcards, tables, and charted graphs. The new service may be utilized in connection with the data processing, programming, and computer services already available through the branch.

The scanning and plotting system consists of two basic components—a curve scanner and a point plotter. A card reader, card punch, and an electric typewriter serve as satellite equipment.

The system was designed for NIH by the Gerber Scientific Instrument Company of New Haven, Conn., and is unique in that the two basic components may be utilized in a single operation combining curve scanning, point plotting, and data capturing. Normally, the two

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## Building Funds Awarded For Research Facilities

PHS Surgeon General Terry has announced the award of 36 health research facilities grants, totaling \$4,696,031, to 32 institutions in 20 States.

These funds, which complete the FY 1961 distribution, include monies temporarily turned back by institutions unable to begin construction before July 1, 1961.

This transfer of funds is in response to President Kennedy's call to speed construction as a stimulant to the national economy. Institutions returning their unused funds will be reimbursed from the 1962 fiscal year budget.

The Health Research Facilities Program awards matching funds to non-profit hospitals, medical and dental schools, schools of public health, and other institutions to build and equip health research facilities. Established on a three-year basis in 1956, the program was extended through FY 1962.

The program is administered by the Division of Research Grants. The Health Research Facilities National Advisory Council recommends grants to the Surgeon General for approval.

## Shannon Cites Need for Higher Pay, More Space at NIH Budget Hearings

Insufficient office space, low professional pay scales, and highlights of research at NIH were among the major subjects discussed by NIH Director James A. Shannon at hearings on the NIH budget for Fiscal Year 1962, conducted by the House Subcommittee of the Committee on Appropriations.

Dr. Shannon pointed out that although the new Office Building, with 173,000 square feet of office space, will probably be ready for partial occupancy late this summer, the continuing expansion of NIH has already committed all of the space. It will therefore be necessary, he said, to continue to house about 1,000 employees in rented space in Bethesda and Silver Spring throughout the next year.

### Problems Listed

Among the problems resulting from this dispersion of activities, Dr. Shannon said, are communication difficulties, transportation delays, and effects on the morale of the off-reservation personnel.

A request for funds for the planning of an additional major office facility on the NIH grounds has been included in the 1962 budget.

The possibility of decentralizing certain of the NIH functions was suggested by Dr. Shannon. A resident extramural staff in San Fran-

(See *SHANNON*, Page 4)

## Terry Commends House Report on Grant Program

An extended study of NIH administration of extramural grants and training programs conducted over the past two years by the House Committee on Government Operations culminated May 1 with release of the Committee report and recommendations.

In a statement issued the following day, PHS Surgeon General Luther L. Terry hailed the report as coming at an opportune time because of the rapid expansion and increasing complexity of NIH extramural activities in recent years.

### Suggestions Welcomed

Dr. Terry's statement follows:

"The House Committee on Government Operations, through its study and report on the research and training programs of the National Institutes of Health, has rendered a service to the National research effort by suggesting measures for strengthening administration. This report comes at an opportune time as the National Institutes of Health moves rapidly into the administration of larger and more complex programs of medical research and training directed by the Congress over the past three years.

"The report of the Committee has pointed out some procedural measures that will be very seriously considered in the interest of economical and businesslike administration. However, in working out these measures, care must be taken that they do not adversely affect the attainment of the essential purpose of the programs—the production of research findings contributing to the conquest of disease."



Irving W. Gillespie manipulates the controls at the console of the curve scanner in Building 12.

## NIH Research Featured in N. Y. Times Series

The New York Times has carried in recent issues a series of articles on NIH and its multiple research activities, which has attracted widespread attention and favorable comment.

Author of the series is Harold M. Schmeck, Jr., who spent several days at NIH in late April interviewing top Institute and Division scientists and administrators.

The first article, which appeared Sunday, April 30, describes the organization, operations, and objectives of NIH.

Succeeding articles which have appeared prior to the *Record's* copy deadline were in the Times issues of May 4, 7, 11, and 14. They described NCI virus research, the various NIH studies related to the aging process, NIAID malaria research, and germfree studies.

# the NIH Record

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## PERSONNEL TO PERSON

The Employee Development Section announces that William L. Fournier, Educational Counselor of George Washington University, will again be available to counsel NIH employees on their educational interests.

Although emphasis will be placed on the forthcoming summer school sessions, Mr. Fournier will also advise employees on their longterm academic plans.

Assistance and counsel will not be limited to any particular field, and Mr. Fournier will have curricular information from the many colleges and universities in the Washington area.

The counseling service will be available, by appointment, on May 26 or June 2, in Bldg. 1, Rm. 114, between 10:30 a.m. and 2:30 p.m.

Interested persons may be scheduled for an appointment for either day by calling the Employee Development Section, Ext. 2147.

### SUBSCRIBER KITS

Blue Cross-Blue Shield has issued "Subscriber Kits" for all employees enrolled in the Government-Wide Service Plan. The kit is designed to aid the user in keeping records of all his medical expenses.

If you are a member of this plan, you may obtain your kit from your Administrative Office or the Employee Relations and Services Section, Bldg. 1, Rm. 21.

It will be necessary for you to show your Blue Cross-Blue Shield identification card.

### Information Office Moves

The Clinical Center Information Office, including its Special Events Section, moved recently to Rooms 1-N-242, 246, and 248 in Building 10. The telephone extensions are the same as before: Ext. 2563 for the Information Section and Ext. 3475 for the Special Events Section.

## Participation Increase In Federal Campaign Cited by Dr. Andrews

Final reports on the Federal Service Joint Crusade and National Health Agencies campaign for 1961 reveal that NIH participation increased 9.3 and 8.6 percent, respectively, over last year.

According to figures released by Dr. Justin M. Andrews, Director of NIAID and Chairman of this year's drive, 59 percent of the employees at NIH participated in the National Health Agency campaign and 57 percent participated in the Federal Service Joint Crusade.

### Sends Letter

In a letter to Institute Directors and Division Chiefs Dr. Andrews said, "It is heartening to note that the NIH participation increased from prior years and with few exceptions the response from the Institutes and Divisions was better this year than heretofore."

Dr. Andrews also commended Division Chairmen and Keymen. "We gratefully acknowledge," he said, "the personal time and effort these people have given to support of the agencies and to help the NIH meet its community responsibility in this endeavor."

A breakdown of the report follows:

Organization	Percent of Participation	
	N.H.A.	J.C.
NIAID	84	81
DBS	82	80
NIDR	81	80
DGMS	81	75
DRS	75	65
NCI	69	65
DRG	65	65
OD-OAM	62	62
NIAMD	49	54
NHI	49	45
NIMH	45	45
CC	41	40
NINDB	39	38

## Research Findings of NIH Investigators Reported at Radiation Society Meeting

Seven papers representing the research findings of 13 NIH investigators were among the reports presented at the Ninth Annual Meeting of the Radiation Research Society at the Sheraton-Park Hotel in Washington, May 15-17.

The principal address at the opening session of the meeting was delivered by Dr. Glenn T. Seaborg, Chairman of the United States Atomic Energy Commission, who spoke on "Research in Atomic Energy."

The program of the three-day meeting consisted of scientific sessions on the biological, chemical, and physical effects of X-rays and other forms of high-energy radiation, and eight symposia.

Symposia dealt with special top-

ics of current interest, including "Late Effects of Ionizing Radiation" and "Solid State Studies in Radiation Damage."

Dr. Mortimer M. Elkind of the Laboratory of Physiology, NCI, was chairman of a symposium on "Molecular Processes and Their Possible Relationship to Radiation Effects," and Dr. Delta E. Uphoff of the Laboratory of Biology, NCI, presided at a scientific session on "Bone Marrow—Transplantation and Immunology."

### Other Participants Listed

Members of the Local Committee for the meeting included Drs. Howard L. Andrews, Chairman; Charles R. Maxwell, and Willie W. Smith, all of the Radiation Branch, NCI.

Authors of NIH papers presented at the scientific sessions, all of NCI, were Dr. Elkind, Willie B. Moses, Harriet Sutton, Dr. William C. Mohler, Dr. Roger J. Berry, Dr. J. Robert Andrews, and Dr. Ruth M. Merwin; Dr. Richard L. Swarm, Eliza Miller, Herman Michelitch; Dr. Peter Riesz, Alton D. Rollins, and Dr. Bernard E. Burr.

The Radiation Research Society, founded in 1952, is a national professional society of biologists, physicists, chemists, and physicians contributing to knowledge of radiations and their effects.

## PHS Awards 7 Grants For Cancer Facilities

The Public Health Service recently announced the awarding of seven grants to institutions for construction of cancer research facilities.

The money will be used to construct, enlarge, or renovate buildings to house research programs already in progress.

The list of approved grants follows:

University of Wisconsin, Madison: New building for McArdle Laboratory, \$2,475,000; 48-bed addition to Cancer Research Hospital, \$448,000.

Temple University, Philadelphia: Completion of unfinished area of biology building \$49,100.

Wistar Institute, Philadelphia: Addition and remodeling, \$284,378.

Johns Hopkins University, Baltimore: Addition to animal house, \$45,000.

University of Texas, M. D. Anderson Hospital, Houston: Remodeling and construction of new facilities in existing building, \$639,213.

University of Washington, Seattle: Construction of facility connecting two wings of existing building, \$1,059,309.

## RADIATION

(Continued from Page 1)

Leukemia P-388 can be transplanted successfully in 50 percent of recipient mice by injection of fluids containing not more than two unirradiated cells. From the information obtained in this way, it is possible to calculate the antitumor effect of various radiation doses.

Two experimental anticancer drugs were studied by this technique, IUDR and BUDR. Although IUDR alone did not inhibit the viability of transplanted P-388 cells, it markedly enhanced their sensitivity to irradiation, so that they failed to produce tumors when injected into other mice. BUDR alone produced moderate inhibition of cell viability, and also potentiated radiation effect at low dose levels of the drug.

### May Prove Valuable

Dr. Andrews suggests that this technique for measuring precisely the tumor-damaging effect of irradiation may prove highly valuable in basic studies of radiation biology and cancer therapy.

It could permit scientists to screen chemicals for their ability to increase the potency of irradiation. Such drugs could be extremely useful in the treatment of human cancer since they would permit effective use of lower irradiation doses.

A second finding reported by Drs. Andrews and Berry was the observation that neutron beam irradiation, not used clinically because of technical obstacles, may offer certain advantages over the widely used X-irradiation.

Under the experimental conditions neutron irradiation produced an antitumor effect equal to that of X-rays administered under oxygen tension. It is well known that increasing the oxygen pressure within a target cell renders the cell more susceptible to X-ray.

## DNA Research Findings Presented in Lecture By French Scientist

Some unexpected physical changes in the basic characteristics of vertebrates, following injections of deoxyribonucleic acid (DNA), were discussed by Dr. Jaques Benoit, Professor of Histophysiology, College de France, Paris, on May 12 in the Clinical Center Auditorium.

The NIAMD-sponsored lecture entitled "Morphological Modifications of the Pekin Duck after Deoxyribonucleic Acid (DNA) Injections," was a report of a pilot study commenced in 1956.

At that time Dr. Benoit and associates were anxious to learn whether investigators could hope to rediscover in vertebrates the results obtained in microorganisms by DNA action.

Dr. Benoit has been an independent investigator in the field of endocrinology since 1919. He holds M.D. and D.Sc. degrees and completed a Rockefeller fellowship during the academic year 1936-37 at Yale University.

He held a professorship in histology at Algiers and in embryology at Strasbourg prior to his present appointment at the College de France.

## Guggenheim Fellowship Awarded to Dr. Bell

Dr. J. Frederick Bell of the NIAID Rocky Mountain Laboratory, Hamilton, Mont., has received a fellowship from the John Simon Guggenheim Memorial Foundation which will permit him to spend two months abroad.

Dr. Bell will study the epidemiology of tularemia. He will consult and conduct field investigations with European investigators and will collect type cultures.

His itinerary includes Belgium, France, Yugoslavia, Austria, and Czechoslovakia. He will also go to Finland, Norway, and Sweden before returning to Hamilton by way of Bethesda at the end of June.

## Annual Barbershop Sing Scheduled for June 7

The annual NIH program of barbershop harmony by the Singing Capital Chorus will be presented Wednesday, June 7, at 8 p.m. in the CC 14th floor auditorium.

The chorus consists of members of the D.C. Chapter of the Society for the Preservation and Encouragement of Barber Shop Quartet Singing in America, Inc.

The chapter's smaller 25-man chorus, the Precisionists, and several quartets will also appear on the program which is being pro-

## Monkey Trapping Supervised To Obtain Healthy Specimens

Expansion of the Division of Biologics Standards' investigation of viruses indigenous to monkeys and monkey kidney tissue cultures, in relation to the epidemiology of virus diseases of monkeys and to the preparation and control of various virus vaccines, is under way in the Laboratory of Viral Immunology. Dr. Gerald L. Van Hoosier, head of the Simian Virus Unit, is in charge of the program.

### Conditions Are Important

Conditions of trapping, as well as handling and shipping, are important factors in obtaining healthy monkeys for use in the poliomyelitis and measles vaccines control programs at DBS.

In order to study these conditions at close range, Dr. Van Hoosier and Dr. Harry M. Meyer,



This Indian trapper is pointing to a wild monkey in a nearby tree. The net in foreground is one of those set up in certain areas for capturing monkeys driven into those areas.



Cages in foreground are conventional bamboo cages used by natives in this part of India for shipping animals to the nearest collection point. The smaller cages at right are special isolation cages taken to India by NIH personnel for containing monkeys captured for special research use.

duced by Robert L. Campbell, Publications & Reports Section, NIMH. The master of ceremonies will be William G. Baylis, Executive Offi-

Jr., members of the Division staff, recently made a trip to the Philippines to obtain blood samples from cynomolgous monkeys, which are being considered for possible use in the vaccine control program, and to India to supervise the trapping and handling of 115 rhesus monkeys from the moment of capture in the "jungle" to their arrival at the NIH.

Dr. Van Hoosier is primarily concerned in the biology and epidemiology of simian viruses in general; Dr. Meyer is investigating two specific viruses and their relation to the monkey—the measles virus and the vacuolating virus.

### Will Study Serum

Dr. Van Hoosier's unit will study the monkey serum specimens in an effort to elucidate the epidemiology of simian viruses in the natural host. These data should provide information as to the source of infection with these agents, as well as to suggest methods of handling to prevent the spread of such infection. Such information is essential to ensuring a supply of healthy monkeys for the production and testing of viral vaccines.

On May 8, Drs. Van Hoosier and Meyer made a brief presentation of their findings to the NII Primate Research Study Section showing slides and movie film of the actual trapping and handling conditions in the Indian State of Uttar Pradesh, situated approximately 150 miles northeast of Delhi.

The work of Dr. Van Hoosier's unit will be directed toward building up a collection of prototype viruses, type specific antisera, and detailed data on the viruses which are encountered in work with monkey tissue.

cer, NIAMD. NIH employees, CC patients and their families and friends are invited to attend.

## Drinking Relationship To Traffic Accidents Studied at Conference

What role does drinking actually play in traffic accidents? How extensive is the problem nationally and worldwide? How effective are enforcement techniques? Does the structure of modern society preclude complete solution of the problem?

Answers to these and other questions relating to the problem of drinking-driving are being discussed and evaluated at the National Conference on Alcohol and Traffic Safety in Pittsburgh, Pa., the first three days of this week.

Major papers by five U.S. speakers and one Canadian and a panel discussion featuring four distinguished foreign scientists will highlight the program.

Dr. Robert H. Felix, Director of the National Institute of Mental Health, delivered one of the two welcoming addresses at the opening session of the conference. The other was delivered by Dr. Albert Chapman, Chief of the Division of Accident Prevention, PHS.

Dr. Chapman also is chairman of the panel discussion, and Dr. Paul V. Joliet, Deputy Chief of the Division of Accident Prevention, will chair the final, plenary session.

## DRG Sponsors Meeting On Occupational Health

A conference on Epidemiologic Research in Occupational Health, sponsored by the Environmental Sciences and Engineering Section, Division of Research Grants, was held here May 10 and 11 in Wilson Hall.

The two-day, four-session meeting consisted of program and round table discussions of the present status of information concerning health problems existing in employed populations and their possible relation to the environmental conditions of occupation.

The conferees also explored research possibilities, means of stimulating research in neglected areas, and ways of overcoming obstacles to medical research in industry.

In addition to members of the Study Section, participants included representatives of the Advisory Committee of the Division of Occupational Health, Federal agencies, labor organizations, industrial management, and educational institutions.

Among these were industrial medical directors, industrial hygiene and sanitary engineers, physiologists, toxicologists, biostatisticians, and epidemiologists.

The conference was supported through a grant from the Division of General Medical Sciences.

## SHANNON

(Continued from Page 1)

cisco to cover the activities of NIH in relation to institutions in the California area is under consideration. A similar idea is suggested for the Boston area.

This would permit the resident staff, according to Dr. Shannon, "to service grants locally and to minimize the number of small decisions that have to be made centrally so that the top staff that remains in Bethesda can be more concerned with the broad decisions than with the followthrough of their implementation."

Too high a proportion of exceptional scientists is being lost to other institutions, Dr. Shannon said, because of "sometimes irresistible inducements."

He cited the conditions for maintaining scientific excellence on the Bethesda campus as "excellence of research facilities, intelligent and considerate administration, due recognition of achievement, opportunities for promotion, and pay scales that will not only withstand comparison with those of the better universities but will to some extent offset the opportunities for supplemental income which attend most university appointments."

### Programs Recommended

A program has been recommended that would increase the incentive and the pay scale of scientists within the Civil Service system. It would also permit temporary detailing of PHS Commissioned Officers to jobs established at a given pay level, permitting a more reasonable compensation for services, without interfering with the officers' long-term benefits under the Career Compensation Act.

Dr. Shannon cited several progress reports on recent work here as examples of the importance of onsite research and of the "acknowledged excellence, imagination, and drive" of NIH scientists. These included:

- The discovery that simian malaria can be transmitted to man by the bite of an infected mosquito, indicating that there may be hitherto unsuspected sources from which humans may be infected by new strains of malaria parasites.

- Evidence, from studies of germfree animals, that a specific micro-organism may be the cause of dental caries, with the implication that immunologic or chemotherapeutic prevention may be possible.

- The discovery (in animal studies) that the interplay between the rates at which cholesterol enters and leaves the wall of major arteries is a significant factor in the development of atherosclerosis.

- The development of a rapid chemical method for measuring the activity of the enzyme, montamine

## 3 Risk Factors in Middle-Aged Men Tend to Heart Disease Development

Men 40 to 60 years of age run almost three times as great a risk of developing coronary heart disease if they have 1) high blood cholesterol level, 2) high blood pressure, or 3) an enlarged left ventricle, as do men in that age group who are normal in these respects.

This finding, reported by National Heart Institute researchers at the recent 42nd Annual Session of the American College of Physicians in Miami Beach, was one of the important results from six years of follow-up in the long term epidemiological study being conducted by the Heart Institute at Framingham, Mass.

### Cross-Section Studied

In this study, a cross-section of the adult residents of the community is being observed over a long period of time to find out how many of them develop heart disease, when it develops, and what factors are associated with it.

The investigators, Drs. W. B. Kannel, T. R. Dawber, A. Kagan, N. Revotskie, and J. Stokes, III, reported also that combinations of any two or all three of the cited abnormalities further increased the risk of coronary disease.

It was found that for men 40 to 60 years of age whose cholesterol level, blood pressure, and left ventricle size were normal, the six-year incidence of coronary heart disease was 36 per thousand. For men in this same age group who had all three abnormalities, however, the incidence rose to approximately 500 per thousand.

Considerable difference between

oxidase, which is of central importance to the understanding of a wide variety of phenomena related to hypertension and mental disorders, as well as of the mechanism by which drugs can modify these disease processes.

- Continued encouraging results in the chemotherapy of uterine choriocarcinoma with massive doses of methotrexate. Of 63 women treated at the Clinical Center, 30 have by now been in complete remission for at least one year, while several have remained free of all evidence of disease for five years.

Other witnesses present at the March 22 Subcommittee hearings were Dr. Luther L. Terry, PHS Surgeon General; Dr. David E. Price, NIH Deputy Director; Dr. G. Burroughs Mider, NIH Director of Laboratories and Clinics; Richard L. Seggel, NIH Executive Officer; Dr. G. Halsey Hunt, Chief, DGMS; Harry L. Doran, Chief Finance Officer, PHS; and James F. Kelly, Budget Officer, DHEW.

the sexes on factors associated with development of coronary disease was revealed in the study. A high blood cholesterol level (245 milligrams percent or above) was associated with a more than three-fold increase in risk among men 40 to 60 years old, but contributed only slightly to an increased risk in women the same age.

On the other hand, high blood pressure was associated with a two-fold risk increase for men as contrasted with a six-fold increase in risk for women.

Other findings further pointed up the significance of the sex differential as a factor. Of the 5,127 persons in the study who did not have coronary heart disease when first examined, 186 developed the disease during the six-year period of observation. Thirty-four were in the age range from 30 to 45, with an incidence ratio of 12 men to one woman. One hundred fifty-two were in the age range from 45 to 60, with the ratio at these older ages decreasing to approximately two men to one woman.

### Severe in Men

The type of coronary disease was found to be more severe in the men than the women. Angina pectoris alone occurred in 70 percent of the women but in only 30 percent of the men. Coronary heart disease in men was chiefly manifested as myocardial infarction or sudden death. Sudden death was four times as common in men as in women.

The investigators also reported that 39 (approximately 45 percent) of the 88 men who developed myocardial infarction during the six years of observation were not hospitalized. Sudden death occurred in one-half of those not hospitalized and another 20 percent of them experienced "silent" infarctions which went unrecognized until revealed by routine electrocardiograms at subsequent regular examinations.

These facts, the investigators stressed, indicate the important place prevention must have in efforts to control coronary heart disease.

### Dr. Backus Appointed Selection Secretary

Dr. Robert C. Backus has been appointed Executive Secretary of the Selection Committee for Senior Fellowships in the Research Fellowships Section of the Research Training Branch of the Division of General Medical Sciences.

Prior to his present appointment, Dr. Backus was with the National Cancer Institute, where he had

## NCI's McLaughlin Wins First Prize for Paper In SAMA Competition

Dr. Edward D. McLaughlin, a Clinical Associate of NCI's Surgery Branch, was awarded first prize in the Scientific Forum of the Student American Medical Association, held early this month in Chicago, for his paper on the demonstration of serum factors influencing cell growth.



Dr. McLaughlin

Dr. McLaughlin's award, consisting of an illuminated plaque and a check for \$500, was presented at the banquet session on May 4.

The paper reported the results of a study to determine the effects of serum from hosts with transplanted and spontaneous tumors upon the rate of mitotic activity and hepatic regeneration in the rat. A biological model consisting of partially hepatectomized white rats was employed, inasmuch as previous workers had shown that the rate of mitosis in regenerating liver is comparable to the rate in most tumors.

### Suppressive Effect Noted

Examination of the sacrificed animals revealed that injection of serum from cancer patients either stimulated or failed to inhibit mitotic activity, while normal serum appeared to exert a suppressive effect in every instance.

An additional finding that serum from animals bearing a transplanted tumor inhibited liver regeneration in the same manner as the serum from normal animals suggested that the factor which leads to increased mitotic activity in the test system is related to changes in the host rather than to the presence of the tumor.

The clinical phase of the investigation was carried out after Dr. McLaughlin's appointment as Clinical Associate here in 1959, and was based on methods developed partly during his previous year as Surgical Resident at Jefferson Medical College. After his Clinical Associate term expires in July, he will remain at NCI for another year as Staff Surgeon.

The Student American Medical Association is sponsored by the American Medical Association, but is separate from the parent organization. Its purpose is to stimulate and recognize research among physicians during the residency phase of their training.

served since 1958 as Executive Secretary to the Cancer Research Training Committee and the Specialty Fellowship Board.

## Krypton Tracer Used In Circulation Study

Presented at the 45th Annual Meeting of the Federation of the American Societies for Experimental Biology.

When radioactive krypton ( $Kr^{85}$ ) is introduced into the blood stream it is eliminated during one trip through the circulatory system either by diffusion into the tissues of the body or by exhalation from the lungs. These properties of  $Kr^{85}$ , as well as the ease with which its concentration in blood and in air can be determined, have made it a useful agent for measuring cerebral blood flow, characterizing circulatory shunts, and studying intrapulmonary ventilation-perfusion relationships.

Studies reported here show that these same characteristics of  $Kr^{85}$  also make it a better agent for measuring cardiac output than those used in standard dye techniques. Dyes cannot be used to measure cardiac blood flow accurately in cases of congestive heart failure or of valvular regurgitation since some dye will remain in the heart and some will be recirculated back to the heart. Since  $Kr^{85}$  does not recirculate, it can be used very satisfactorily in these cases. In patients with circulatory shunts  $Kr^{85}$  can be used to determine separately right and left ventricular outputs, and thus to assess the magnitude of the shunt.

### Method Is Simple

The  $Kr^{85}$  technique is a simpler method than the standard dye techniques, requiring less blood, fewer instruments, and less calculation.  $Kr^{85}$  may be injected into the left side of the heart and measured in a single blood sample withdrawn at a constant rate from a systemic artery, or injected into a vein and measured in a sample withdrawn from the pulmonary artery. Only the primary time-concentration curve is obtained since recirculation of  $Kr^{85}$  is negligible. The Stewart-Hamilton formula, a method of calculating blood flow, can be used to determine ventricular output when the amount of indicator injected, its mean concentration during the sampling period, and the exact duration of this period are all known.

The accuracy of this technique was tested in three different series of experiments by Drs. William P. Cornell, Eugene Braunwald, and Edwin C. Brockenbrough of the National Heart Institute. In 27 experiments using a circulatory model, flow rates of water through the mixing chamber determined by the  $Kr^{85}$  technique averaged 0.7 percent less than the actual flow rates, with a maximum difference of 11.3 percent. In 26 comparisons of cardiac output in dogs, the output as

## Cash Prizes Awarded to Five Entries In Third Annual Art Exhibition Here



Four of the winners in the Third Annual NIH Art Exhibit, sponsored by R&W, are shown with their entries. From left: Anita Wertheim with her oil painting, "Boats and Docks"; Dr. Hans J. Cahnmann with his watercolor, "Street Burgogne-Sur-Seine"; Michael S. Murtaugh with his sketch, "Three Nuns" (on left panel); and Jennie Lea Knight with her oil, "Euripedes." Also shown are two other winning entries: on center panel, "Chesapeake and Ohio Canal at Georgetown," an etching by Inez Demonet (2nd prize); and the print, "Bread," by Dr. Frank McClure (Hon. Ment.). The exhibit will be on display in the CC lobby through June 11.

The Third Annual NIH Art Exhibit, sponsored by R&W, opened Sunday, May 14, in the lobby of the Clinical Center and will continue on display through June 11.

Cash prizes were awarded to five winners for their entries in two general categories—oil paintings and the graphic arts.

Judges of the entries were William Calfee and Robert Gates, instructors in art at American University, and Dan Turano, well-known sculptor and teacher associated with the Corcoran Gallery of Art.

They evaluated 165 items before selecting 48—oils, graphics and sculpture—for display.

Dr. Harold P. Morris of NCI, President of R&W, presented the awards at the opening of the exhibit.

Jennie Lea Knight, Laboratory of Psychology, NIMH, received the first prize of \$50 in the oil paint-

determined by the  $Kr^{85}$  technique averaged 5.2 percent greater than the output as determined by the rotameter, a flow-rate meter. The maximum difference was 26.1 percent. In 19 comparisons of cardiac output in patients, the output as determined by the  $Kr^{85}$  technique averaged 1.5 percent greater than the output as determined by the cardio-green dye dilution method, with a maximum difference of 11.0 percent.

ing division for her abstract, "Euripedes." A second award of \$25 went to Anita Wertheim, also of NIMH, for her scene, "Boats and Docks."

In the graphic art division, Michael S. Murtaugh, son of Joseph S. Murtaugh, Chief of the Office of Program Planning, OD, was awarded the first prize of \$50 for his drawing, "Three Nuns." Inez Demonet, of the Scientific Reports Branch, DRS, won second prize and \$25 for her etching, "Chesapeake and Ohio Canal at Georgetown," and Dr. Hans J. Cahnmann, Clinical Endocrinology Branch, NIAMD, won third prize of \$10 for his watercolor, "Street Bourgogne-Sur-Seine."

Dr. Frank McClure, Laboratory of Biochemistry, NIDR, received honorable mention for his print, "Bread."

The exhibit is open daily to the public from 9 a.m. to 9 p.m.

### Dr. Goodman Presents Paper at Monte Carlo

Dr. Howard C. Goodman, Head of the Clinical Immunology Section of the Laboratory of Immunology, NIAID, presented a paper at a symposium on "Advances in the Laboratory Demonstration of Antibody-Antigen Reactions," held at Monte Carlo early this month.

The symposium was sponsored by the Council for International Organizations of Medical Science.

## NCI Scientists Report Red Cell Output Drop From X-Ray Therapy

An understanding of the effects of whole-body irradiation is essential in view of tests of nuclear weapons, exploration of outer space, and accidental industrial exposure. Furthermore, whole-body irradiation is now in experimental use as therapy for certain inoperable forms of cancer.

Some data on the effects of this therapy on production of red blood cells by the bone marrow have now been reported by scientists of the National Cancer Institute's Radiation and General Medicine Branches.

The activity of bone marrow was determined indirectly through the use of radioactive iron as a marker. The rationale is that the rate at which iron disappears from the plasma is a measure of its utilization in the formation of hemoglobin, the oxygen-carrying component of red cells.

### CC Patients Studied

The subjects of the study were ten patients admitted to the Clinical Center with disseminated lymphomas and chronic lymphatic leukemia. Small amounts of radioactive iron were injected intravenously, and the rate of disappearance was determined to establish a control level for each patient. Then, doses of 80 to 100 roentgens of whole-body irradiation with 2-million electron volt X-rays were given as initial therapy.

The rate at which radioactive iron disappeared dropped significantly below control levels in all patients, thus reflecting a fall in production of red cells. The rate was lowest two to three days after irradiation, and returned to control levels by the eighth day. This initial decrease preceded any change in the numbers of circulating red cells.

### Second Decrease Occurs

A second, and in some instances greater, decrease occurred between the twenty-second and twenty-eighth days in six patients studied during this period. This suggested that the effects of radiation on production of red cells last longer than was previously suspected.

Another interesting observation in this study was the extent and long duration of remissions induced by 100 roentgens of whole-body irradiation.

The report, which appears in a recent issue of *The Journal of Clinical Investigation*, was written by Drs. Jack Levin, now with the Yale Medical School; J. Robert Andrews, Chief, Radiation Branch; and Nathaniel I. Berlin, formerly Chief, General Medicine Branch, now Clinical Director, NCI.

## New Evidence Indicates Tumor Rejection Cause May Be Tissue Antigen

A new function for cells known as oligodendrocytes has been proposed by a National Institute of Neurological Diseases and Blindness scientist, who offers anatomical evidence that these cells may be involved in the regulation of intrinsic blood flow to neurons of the brain and spinal cord.

Oligodendrocytes, which are enclosed in the web of tissue supporting nerves (neuroglia), were previously thought to regulate the metabolism of nerve cells and myelin.

Dr. Jan Cammermeyer, Laboratory of Neuroanatomical Sciences, NINDB, however, has observed the tendency of oligodendrocytes to cluster exclusively along blood vessels and near neurons of both gray and white nerve tissue. He theorized that the unique arrangement and strategic location of these cells might enable them to control vascular diameter and blood flow in some regions of the central nervous system.

This theory was substantiated by recent findings of other investigators that oligodendrocytes connect with neurons by means of delicate nerve fibers and synaptic contacts, and exhibit a rhythmic contractility suggesting a dynamic function.

### Variation Noted

Recent observations by Dr. Cammermeyer have shown that the arrangement of oligodendrocytes varies considerably in different areas of the brain and in different mammalian species.

Knowledge of the normal variations is paramount for a correct interpretation of pathologic changes. This variability may also indicate that the extent of blood flow control by the oligodendrocytes is adjusted to the needs of both individual neurons and regions, thus insuring the most economical distribution of blood.

An interesting correlation was found between the distribution of oligodendrocytes and the location of areas of brain damage. Certain disease processes which interfere with the local blood supply appeared in some instances to affect areas rich in oligodendrocytes; in other instances, areas with few of the cells were damaged.

Therefore, the arrangement or content of oligodendrocytes may contribute to the variations in susceptibility of gray and white matter to either anoxia or toxic agents, as well as to the unique localization of certain disease processes.

As a consequence of these studies, new leads for future research have been suggested. Further investigations may concern the complex of

## Transventricular Mitral Valve Dilatation Held Superior Method in Heart Surgery

Separating the fused (stenosed) lips of mitral valves with a dilating instrument passed through the left ventricle is safer and far more effective than valve-splitting operations utilizing the transatrial approach, Drs. Andrew G. Morrow and Nina S. Braunwald of the National Heart Institute's Clinic of Surgery have reported.

Transventricular mitral commissurotomy was devised in 1954 by Andrew Logan, of Edinburgh, Scotland. The procedure is almost universally employed in the United Kingdom, but has received scant attention in this country. The NHI Clinic of Surgery adopted the technique in 1958, because of the inadequate operative results obtained in many patients by the transatrial approach.

As currently practiced in this clinic, mitral commissurotomy involves an initial attempt to open the valve digitally, through the left atrium. If this is not feasible, then a two-bladed dilator is inserted through an incision in the heart's apex, passed through the left ventricle, and positioned in the mitral orifice by the surgeon's finger, which remains in the atrium to assess the results of dilatation.

Although palpation indicated that complete separation of the valve leaflets was easily accomplished and that mitral insuffi-

ciency was neither produced, nor, if already present, aggravated by transventricular dilatation, pre- and postoperative measurements of the abnormal pressure gradient across the valve provided a more objective evaluation of the technique.

Such pre- and postoperative measurements were obtained from 25 patients subjected to transventricular dilatation and compared to similar data obtained from 50 control patients whose valves were opened (prior to adoption of the transventricular technique) digitally, or by use of a knife passed through the atrium. Results of this study were reported in the *Journal of Thoracic and Cardiovascular Surgery*.

The studies showed that reduction of the pressure gradient to less than 8 mm. Hg., considered an indication of satisfactory relief from stenosis, was accomplished in 20 (80%) of the patients subjected to transventricular commissurotomy, but in only 26 (52%) of the control patients.

"The results of the study indicate that transventricular mitral commissurotomy is a safe and practical technique and effectively relieves mitral obstruction with minimal risk," conclude Drs. Morrow and Braunwald. They also state that the technique will undoubtedly be more widely used as its advantages become better known.

## Drs. Pastan and Field Win Van Meter Prize

Drs. James B. Field and Ira Pastan of NIAMD's Clinical Endocrinology Branch were awarded the 1961 Van Meter Prize of the American Goiter Association for their paper entitled "Studies on the Mechanism of Action of Thyroid Stimulating Hormone."

The prize of \$300 was accepted by Dr. Field at the Association's annual banquet in Philadelphia May 3.

The Van Meter Prize is offered annually by the American Goiter Association for the best manuscript covering original and unpublished work on goiter, especially its basic causes. Drs. Field and Pastan reported on their findings concerning the biochemical mechanism by which the pituitary gland controls the activity of the thyroid.

factors which may activate these groups of cells, as well as the mechanisms by which they may regulate blood flow.

The studies were first presented at the Seventh Conference on Microcirculatory Physiology and Pathology. Subsequent work appeared in the *American Journal of Anatomy*.

## SCANNING

(Continued from Page 1)

will be used separately.

The curve scanner produces four digits of information for each of the X-Y coordinate values designated on a curve. The coordinate values are located by manipulation of crosshair guides placed at any desired point on the curve. The information obtained is simultaneously punched into cards acceptable as input on automatic data processing equipment.

Attached to the curve scanner are mechanisms for reading graphs on film or on rolls or opaque paper. The point plotter electromechanically reproduces graphs on virtually any desired scale or coordinate system from the punched cards.

Up to six individually identified graphs, each on a different scale, may be plotted simultaneously. Six symbols are available for identification purposes, including the period (.), asterisk (\*), and plus sign (+). All graphs produced will be suitable for any desired reproduction process.

All prospective users are invited to discuss the technical details of the system with Benjamin Baker (Ext. 2282 or 4648) and to inspect the equipment in Rm. G-728, Bldg.

## NIH Research Links Nerve Fibers, Vision

Recent National Institute of Neurological Diseases and Blindness studies indicate that inhibitory, as well as excitatory, nerve fibers lead from the thalamus to the visual center of the brain's cerebral cortex.

Recordings of the electrical activity of single brain cells, after thalamic stimulation, showed evidence of both excitatory and inhibitory activity. These results suggest that the process of inhibition may play an important role in regulating visual function.

In order to study brain cell activity, electrical stimulation was applied to the lateral geniculate body, a thalamic center which receives impulses from the eye and relays them to the brain. The response of cells in the visual cortex was simultaneously recorded by intracellular electrodes and by electrodes on the brain's surface.

### Responses Recorded

The experiments demonstrated that hyperpolarization was an outstanding feature of the responses recorded from neurones in the visual cortex. Hyperpolarization potentials are found when a cell's electrical activity is suppressed or inhibited; depolarization is accompanied by the repetitive firing of an excited cell.

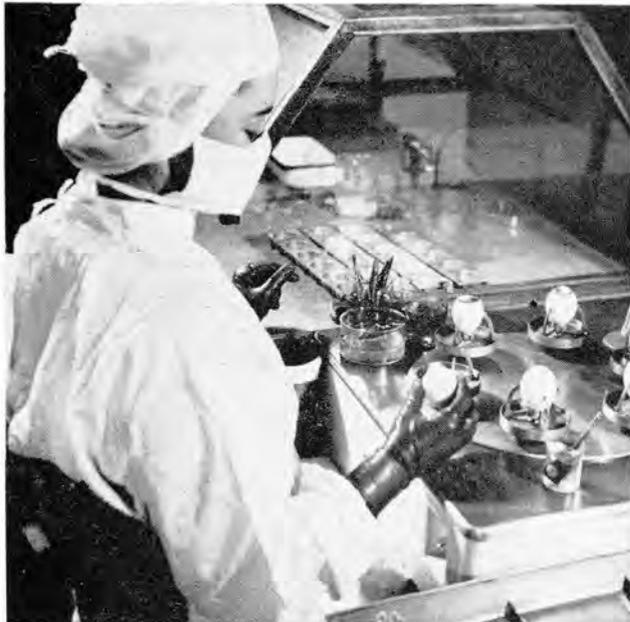
Immediately after stimulation of the lateral geniculate body, many cortical cells showed an initial excitation and depolarization, followed by inhibition and hyperpolarization. Therefore, the stimulus may have activated both excitatory and inhibitory impulses, but the excitatory impulses arrived at the cell more quickly.

In some cases, initial excitation was obscured by an inhibition, and the response consisted of a small depolarization potential followed by hyperpolarization. Other neurones exhibited only hyperpolarization.

Previous studies by other investigators have indicated that inhibitory processes may also affect the activity of spinal motor neurones and the stretch receptor cells. In addition, inhibitory areas have been demonstrated in the cat retina. The present investigations were conducted by Drs. Choh-Luh, Li, Armando Ortiz-Galvin, Shelley N. Chou, and Saxton Y. Howard (deceased) of the Surgical Neurology Branch, NINDB. The results were reported in the *Journal of Neurophysiology*.

12. Both the mathematician in charge, Gayle S. Hueston, and the system operator, Irving W. Gillispie, have received special training in operation of the equipment.

## Rocky Mountain Lab Studies Insect-Borne Diseases



Work of the Rocky Mountain Laboratory in Hamilton, Mont., is shown in this third in the series of picture stories on NIH field stations. A part of the National Institute of Allergy and Infectious Diseases, the Laboratory is now a world center for research on rickettsial diseases, including Q fever, on Colorado tick fever, and on mosquito-borne diseases such as Western Equine encephalitis. Other insect-borne diseases and fungus infections are under investigation. Left to right, top row: dragging for ticks

at Nine Mile area, Missoula, Mont.; buffalo lie stricken with tick paralysis. Middle row: a technician harvests typhus-infected tissue from embryonated eggs; Rocky Mountain wood ticks ingest bacteria or virus-infected media through capillary tubes; and mosquitoes are identified and tested for infectivity. Bottom row: a RML public health nurse collects epidemiologic data on Q fever from dairy operators; mice are reared in the Laboratory's animal department; and bats are collected and banded for a rabies survey.

## Aging Patient Discussed In New DGMS Booklet

A transcription, in booklet form, of a panel discussion on The Aging Patient, conducted at the Fifth Congress of the International Association of Gerontology in San Francisco last August, was published recently by the Center for Aging Research, Division of General Medical Sciences.

Prepared by the Voice of Medicine, the recorded medical journal of the Excerpta Medica Foundation, the transcribed discussion covers topics ranging from therapeutic and dietary needs of the older patient to special examination and diagnostic procedures.

### Moderates Panel

Dr. Geoffrey H. Bourne, Professor and Chairman of the Department of Anatomy, Emory University, was the panel moderator. Panel participants were Drs. Joseph T. Freeman, President of the Gerontological Society, Inc.; Albert R. Behnke, Jr., Director of the Institute of Applied Biology, Presbyterian Medical Center, San Francisco; Nathan W. Shock, Gerontology Branch, National Heart Institute; and Joseph H. Gerber, Director, and Stanley R. Mohler, Medical Officer, Center for Aging Research, DGMS.

Copies of the booklet are available without charge from the Information Office of the Center for Aging Research, Trunnell Bldg., Rm. 111, Ext. 4121.

## Briton Reports Study At Neurology Seminar

Dr. Raymond W. Guillery of University College, London, England, was guest lecturer at an NINDB Laboratory of Neuroanatomical Sciences seminar held May 9 in the Clinical Center.

Using electron-microscopy slides to illustrate his lecture, "Synaptic Structure and its Alteration with Environmental Temperatures," Dr. Guillery described his findings in a study of a small species of lizard found in Italy.

### Prepares Tissue Sections

After maintaining the lizard for varying, controlled periods of time in a cool environment of 19° C. (Typical American room temperature is 21° C.) and a hot environment of 33° C., Dr. Guillery prepared brain tissue sections for electron microscopy examination.

The results of his examinations showed a clear correlation between changes in environmental temperature and changes in two structures within the terminal parts of nerve axons: neurofibrillae and mitochondria.

## DE-SCENTED SKUNKS ARE SWEET



A DE-SCENTED SKUNK is a de-lightful pet, according to John Borzi, Anne Gates, and Barbara Penney (left to right). These three DRS employees learned of a common interest in an uncommon pet when John acquired Anne's skunk "Flower" for his sister's children, and Barbara, a research technician in the NIH Animal Hospital, was consulted on care and feeding. "Posey Polecat" entered Barbara's life two years ago, and obviously responds to tender loving care. Posey, a female, lives out of doors—caged, of course, so that she won't leave overnight. A nocturnal animal of the weasel family, the skunk hibernates from November to March but eats through "mountains of food" in the summer.—Photos by Sam Silverman.

## NIH Cited for High Quality Housing Provided for Dogs Used in Research

A recently revised edition of a PHS brochure, The Dog in Medical Research, cites NIH for providing the best type of housing for dogs used in laboratory research.

The brochure quotes a statement by Christine Stevens, President of the Animal Welfare Institute, pointing out the factors which make the inside kennel and individual outside runway arrangement, as used at NIH, the preferred method for housing dogs.

These factors include ease in cleaning to keep the floors free of parasites, fungi, and bacteria; prevention of the spread of communicable diseases among the animal colony; and the avoidance of dog-fights.

The brochure, published under sponsorship of the Division of Research Grants, presents standards, both physical and ethical, for care and maintenance of dogs used for experiments in medical research.

This third edition of the booklet was revised by Dr. Keith S. Grim-

son, Professor of Surgery at Duke University and Chairman of the Committee on Revision, Surgery Study Section, DRG.

Also serving on the committee were two other Study Section members: Dr. Carl A. Moyer, Professor of Surgery, Washington University, and Dr. Jonathan E. Rhoads, Professor of Surgery at the University of Pennsylvania.

Contents include sections on sources of animals; selection for special purposes; care and handling; quarters; feeding, and humane treatment.

A list of guiding principles is featured, as well as a model pound law for local jurisdiction. New features are the section on humane treatment and a list of organizations interested in the care of laboratory animals.

The brochure—PHS Publication No. 312, Revised 1961—is available at 15 cents per copy from the Superintendent of Documents, U.S. Government Printing Office, Washington 25, D.C.

## PSB Issues Handbook on Safety Regulations

A handbook of NIH safety regulations, the Safety and Fire-Prevention Guide (Plant Safety Handbook No. 1), was issued recently to supervisors here for the information of NIH employees. Copies are also being distributed to new

employees through the Personnel Office.

Prepared by James B. Black, Safety Officer of the Plant Safety Branch, OD, the 19-page, illustrated booklet lists general and laboratory safety and fire prevention regula-

## New Evidence Suggests Certain Cells Regulate Blood Flow to Neurons

Evidence to date points to the presence of a new tissue antigen in mouse polyoma tumor that differs from that present in normal mouse tissues.

Dr. Karl Habel, Chief of the Laboratory of Biology of Viruses, National Institute of Allergy and Infectious Diseases, reported at the 15th Annual Meeting of the Federation of American Societies for Experimental Biology, that this different antigen acts as a foreign substance to which the normal immunologically competent adult animal reacts.

### Theories Postulated

Dr. Habel postulates from his studies of the mouse polyoma virus that when this virus causes tumors in newborn animals these young animals, being immunologically immature, do not recognize the new antigen as foreign. Thus they become tolerant to it and allow the tumor to develop.

When virus is inoculated into the adult animal, some cells are also transformed to tumor cells but the immunologically competent adult recognizes the new tumor antigen as foreign and rejects it. In the process of this rejection in which no tumor develops, the adult mouse becomes sensitized to the new antigen, thus allowing more efficient rejection by the animal of the transplanted tumor with its same foreign antigen when it is inoculated later.

### Resistance Relative

Resistance to supporting the growth of the transplantable tumor is relative and can be overcome by a large dose of transplanted tumor cells. Furthermore, resistance seems to be specific against only tumors originally produced by the polyoma virus. It appears to reside in the cells of the virus-immune adult and is not based on antibodies against the virus itself which are in the blood.

The hypothesis that there is a new tissue antigen in mouse polyoma tumors which immunologically immature animals do not recognize, would explain why the same virus infecting a very young animal results in tumors but in adults causes only inapparent infection with no tumors.

tions at NIH and the reasons for their observance.

In addition, four appendices describe various hazards peculiar to research and industrial institutions and means of prevention.

Copies of the handbook may be obtained from Margaret E. Hargett, Plant Safety Branch, Bldg. 8, Rm. 200, Ext. 4245.