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Michael J. Welch, Ph.D., Recipient of the Aebersold Award

Aebersold Award To Dr. Michael J. Welch

Note from the Director of Mallinckrodt Institute, Ronald G. Evens, M.D.

The following article announces the awarding of a prestigious honor to Michael J. Welch, Ph.D., Professor of Radiology at the Mallinckrodt Institute and Washington University. This is the highest recognition for science bestowed by the Society of Nuclear Medicine. Mike Welch's recognition is well-deserved because of his many contributions to the development of short-lived radiopharmaceuticals, their clinical use, and the training of many scientists in this field. The Mallinckrodt Institute and Washington University take great pride in the recognition of Dr. Welch and are particularly pleased that two of only eight recipients of the Aebersold Award are from this Institution.

The Society of Nuclear Medicine has honored Dr. Michael J. Welch, Professor of Radiology and Chemistry at Mallinckrodt Institute and Washington University for his pioneering role as the first hot-atom chemist to become involved in using a cyclotron to make very short-lived radio-pharmaceuticals for nuclear medicine. Dr. Welch is the recipient of the Society's prestigious Paul C. Aebersold Award which was presented to him at the 27th annual meeting of the Society of Nuclear Medicine, June 24-27, in Detroit.

The Society of Nuclear Medicine is an organization of more than 10,000 physicians, scientists, and technologists. In selecting Dr. Welch, the awards committee took into consideration not only his extensive research contributions in radiopharmaceutical chemistry, but also his equally noteworthy efforts in clinical research, patient care, and teaching.

Other recipients, since the award was first presented in 1973, include Dr. Michel Ter-Pogossian (1976) for the development of the Positron Emission Transverse Tomography (PETT) system, making Mallinckrodt the only medical institution with two recipients. This year, the award includes a plaque of citation praising Dr. Welch for his outstanding achievements in basic science applied to nuclear medicine.



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Dr. Welch was awarded the B.A. and M.A. degrees from Cambridge University, England. In 1965, having received his Ph.D. degree on the chemistry of hot tritium atoms from the University of London, he went on to Brookhaven National Laboratory to begin a two year fellowship with Alfred P. Wolf, studying the chemistry of hot carbon atoms. Entering the field of nuclear medicine in 1967, when he joined the staff of Mallinckrodt Institute of Radiology, Dr. Welch began an effective, far-sighted program of research involving short-lived cyclotron-produced radiopharmaceuticals. As a result, the Institute can count several firsts in the clinical use of positron emitters. Dr. Welch's early research led to the production of simple molecules synthesized directly in the cyclotron target, but by utilizing clever techniques, he soon was able to synthesize more complex radiopharmaceuticals for application in nuclear medicine. His C-glucose for the measurement of cerebral metabolism synthesis represents a benchmark study in nuclear medicine. For the first time, a cyclotron was used to prepare a precursor which was used for biosynthesis of a complex molecule.

During the past decade, one of the most important products developed in Dr. Welch's laboratory has been C-methylputrescine, the first positron emitting radiopharmaceutical for tumor location, which has been used successfully in detecting carcinoma.

The C-palmitate developed in Dr. Welch's laboratory is another radiopharmaceutical involving new and creative cyclotron radiochemistry and is now being used for routine diagnostic PETT imaging, and for the measurement of myocardial metabolism. Demonstrating the clinical efficacy of radiopharmaceuticals such as these, Dr. Welch has facilitated the transition of nuclear medicine away from the determination of organ structure towards the measurement of organ function.

Washington University has been a Specialized Center of Research for thrombosis for ten years, and one major area of achievement has been the success of Dr. Welch and his co-workers in developing pharmaceuticals for studying coagulation disorders. The In-111 research at Mallinckrodt Institute revolutionized the methodology for labeling cells and introduced a whole new class of radiopharmaceuticals to nuclear medicine. Presently, many other laboratories are imitating Dr. Welch's research program involving the use of 111 In-platelets for imaging thrombi and 111 In-leukocytes to detect abscesses and measure inflammatory response in ischemic myocardium.

Early in 1970, Dr. Welch began to develop an interdisciplinary teaching program which today attracts students from across the United States. Prior to its initiation, a career in radiopharmaceutical chemistry required a Ph.D. degree in hot atom chemistry followed by an applied post-doctoral fellowship in a clinical environment. Dr. Welch, in seeking a joint appointment at Washington University in both radiology and chemistry, altered the educational patterns of radiopharmaceutical scientists, demonstrated that the principles of radiochemistry and radiopharmaceutical chemistry could be part of one integrated program, and served as an early role model for the interdisciplinary scientist who applies the rigor of basic science to the solution of practical clinical problems.

Having worked in Dr. Welch's laboratory as a post-doctoral fellow, Kenneth A. Krohn, Ph.D., Associate Professor of Radiology and Acting Director of Nuclear Medicine at the University of California, Davis, comments in a letter supporting the nomination on the dominant role Dr. Welch has played in training graduate students, post-doctoral fellows, nuclear medicine residents, and sabbatical academicians. Included among those scientists are Michael D. Loberg, Ph.D., Director of Pharmaceutical Research, Squibb Institute; John Harwig, Ph.D., Associate Professor, U.S.C.; Mathew Thakur, Ph.D., Associate Professor, Yale University; Linda Knight, Ph.D., Associate Professor, Temple University; and James Frost, M.D., Ph.D., Johns Hopkins University.



Pictured right are former students and colleagues of Dr. Welch. Left to right are: Linda Knight, Ph.D., Temple University; Barbara Francis, George Washington University; William Eckelman, Ph.D., George Washington University; Mathew Thakur, Ph.D., Yale University; Maria Straatman, M.S., Cyclotron Corporation; and Kenneth Krohn, Ph.D., University of California.

Aebersold Award

The Paul C. Aebersold Award honors the memory of a man who was responsible more than any other individual for the acceptance and application of radioisotopes in this country. Dr. Aebersold was a member of a group of scientists under Professor Ernest Lawrence at Berkeley who developed the cyclotron in the early 1930s. He later participated in the production and application of the first radioactive material administered to human beings. Assigned to radioisotope production on the Manhattan Project during World War II and the subsequent development of the atomic bomb, Dr. Aebersold directed the first peaceful distribution and use of radioisotopes at Oak Ridge, Tennessee, In 1946, Mallinckrodt Institute of Radiology shared in the use of an isotope for cancer research when the first unit of radioactive Carbon-14 was released by the War Department to Barnard Free Skin and Cancer Hospital, When Dr. Aebersold retired as Director of the AEC Division of Isotopes Development in 1965, as a result of his efforts, radioisotopes had been applied in the fields of biology, medicine, industry, agriculture, and many others.

The hallmarks of Dr. Michael Welch's career as a research scientist—the importance of a good scientific background, the need to be scientifically adventurous, and above all a propensity for continuing education—represent a fitting tribute to the memory of Paul C. Aebersold.

Elected to Executive Council

Dr. Ronald G. Evens, Elizabeth Mallinckrodt Professor and Director of the Mallinckrodt Institute of Radiology, Washington University School of Medicine, has been elected for a five-year term to the Executive Council of the American Roentgen Ray Society.

The twenty-member Council is the governing body of the Society and includes the officers, the chairmen of key committees, and five elected members.

The oldest of the American scientific radiological organizations, the American Roentgen Ray Society was founded in 1900 in St. Louis with the objective of advancing medicine through the science of radiology. It gives particular emphasis to significant teaching efforts and contributions of members to medical, literature.

Dr. Evens was appointed head of the Department of Radiology at Washington University in 1971. He is past president of the Society of the Chairmen of Academic Radiology Departments, a Fellow of the American College of Radiology, and past president of the Missouri Radiological Society.



Dr. Lin Awarded Grant

Dr. Hsiu-san Lin of the Division of Radiation Oncology has been awarded \$448,053 from the National Heart, Lung, and Blood Institute to continue his investigation on the biology of pulmonary alveolar macrophages for the next five years. Dr. Lin also received a new three-year grant totaling \$126,220 from the National Institute of Allergy and Infectious Diseases to study the origin and differentiation of blood monocytes.

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1980 Gridiron Proceeds For Cancer Research at MIR



Ms. Nancy Belt, 1979-80 President of the Advertising Federation of St. Louis, presents the proceeds of the Gridiron Show to Mr. Edwin B. Meissner, Jr., President of the Board of Directors, Barnard Hospital.

"Grand Slams," the 46th annual Gridiron Show of the Advertising Federation of St. Louis, roasting local personalities and poking fun at the happenings of the previous year, was staged on March 26, in the Khorassan Room of the Chase Park Plaza Hotel. The gala event raised \$13,000 for the Barnard Free Skin and Cancer Hospital, and the funds will be used for further development of the flow-cytometry facility operated by the Mallinckrodt Institute Division of Radiation Oncology, Section of Cancer Biology. This intriguing new technology, which automatically identifies and separates different types of cells in a tissue sample, will greatly speed up the evaluation of new cancer treatments that may be used in future patients.

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Ms. Nancy Belt, 1979-80 AFSL President, made the presentation to Edwin B. Meissner, Jr., Chairman of the Barnard Hospital Board, at a dinner on May 6, at Stan and Biggies restaurant.



Dr. Carlos Perez, Director of the Division of Radiation Oncology at Mallinckrodt Institute, gave a short slide presentation describing the research projects planned for the flow-cytometry facility.

The total AFSL donation to cancer research, since 1945, amounts to over

\$426,000 and, according to Henrietta Meier, Gridiron general chairman, the funds raised have been seed money for matching grants resulting in more than \$1 million in contributions to local cancer research. AFSL's 207-membership includes individuals with interests in advertising and public relations.

FLOW CYTOMETRY

New Technology Holds Possibilities for Cancer Research

The Section of Cancer Biology, Division of Radiation Oncology has recently purchased a Becton-Dickinson, fluorescent-activated cell sorter (Flow Cytometer). This was made possible with a generous contribution from the Advertising Federation of St. Louis. The Flow Cytometer is the heart of an extensive and newly constructed Flow Cytometry Facility at 4511 Forest Park Blvd. that is under the direction of Dr. Alexander Nakeff. The total cost of the unit is \$125,000 and the computer capabilities required to process and analyze the data are worth an additional \$75,000. In addition, the operation of this facility will cost \$94,000 per year.

The Division and Washington University School of Medicine have firmly committed themselves to the development of this sophisticated technology, which will greatly contribute to the cancer research program at Washington University.

Flow cytometry is a new and exciting technology which applies the most recent advances in electronics and laser technology to the solution of some of the most basic problems of cell and tumor biology. A cell suspension must first be mixed with various fluorescent probes (either dyes or labeled proteins, for example) which either bind to the membranes of specific cells of interest or enter them to bind to specific internal structures such as their nuclei. The cells are then introduced into the machine in a stream and pass one-by-one through a laser beam at the rate of thousands of cells per second. Only those cells containing the dye are excited to emit a pulse of light. The signal is detected by photo-sensors which convert this into an electrical signal for storage into computer memory. Subsequently, the cell stream is charged and broken into droplets. Only individual droplets containing a single fluorescently-tagged cell are electically charged and are deflected into collection vessels. Cell analysis and sorting occurs at rates in excess of 1000 cells per second. The Flow Cytometer can examine up to 3 parameters per cell simultaneously with an extension to 5 parameters being readily available. All of the analysis and sorting can also be done without affecting the viability of the cells collected.

There are a number of major areas where flow cytometry will have an immediate and substantial impact on the Divisions' cancer research program. One involves the analysis of different cell subpopulations which are responsible for tumor growth within both human and experimental solid tumors. These can now be separated by flow cytometry based upon their unique staining characteristics with various fluorescent probes. They are being studied following either radiation or drugs or their combination to determine which anticancer treatments are most effective in arresting tumor growth in the development of new and better treatments for cancer.

Many anticancer drugs kill tumor cells most efficiently when the cells are in a drug-sensitive part of their life cycle. One of the major strategies in chemotherapy is to use two drugs in combination. The first drug kills some of the cells, but also arrests the remaining cells in a phase where they will be sensitive to a second drug. Flow cytometry with DNA staining and life cycle analysis is being used to determine which cells were killed by the first agent and, therefore, which cells comprise the target populations for the second agent. This information will enable lower doses of drugs to be administered while maintaining high levels of tumor cell killing and thus contribute significantly to improved combination anticancer drug therapy.

A number of human tumors such as from breast, uterus and prostate are dependent upon specific hormones for their growth. Prior to the advent of flow cytometry, it was no possible to isolate those tumor cells that were hormone-sensitive even though their presence in the tumor and their content of specific hormone receptors was known. The development of fluorescently-tagged hormones such as estrogen and progesterone permits detailed studies of their binding to those target tumor cells expressing the appropriate receptors. Furthermore, the isolation of these cells by flow cytometry and their growth in tissue culture is being used to determine whether they are the same cells responsible for the growth of the tumor.

Immunotherapy is a promising area of cancer research that involves studies of our body's normal defense against malignant cell growth with the goal of boosting this anticancer action to eradicate tumors completely. Flow cytometry together with the development of many highly-specific membrane labels for a host of different types of immune cells is making possible for the first time detailed studies of their interaction with malignant cells within tumors.

It is clear that potential applications of the technology are multiple, being restricted solely by scientific ingenuity. Flow cytometry is so new and different from conventional methods of cell analysis that the full realization of its potential presently lags behind its capabilities.

Multiparameter cell analysis is bringing together cell biologists and clinicians as well as physicists and computer experts in an increasing number of the leading research and treatment centers in the world that now have this capability. The new Flow Cytometry Facility places us on the leading edge of new developments in this important area. It serves as a focus for many of the activities and interests of the Division of Radiation Oncology and creates opportunities for fruitful collaboration with researchers throughout Washington University. Since the Flow Cytometry Facility is the first of its kind in the Bi-state region, provisions have been made for sharing this important resource and facility with other cell biologists and clinical oncologists throughout this region.

MEDICAL

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International Symposium

Michael J. Welch, Ph.D., Professor of Radiology and Chemistry at the Mallinckrodt Institute of Radiology, was Chairman of the Third International Symposium on Radiopharmaceutical Chemistry, hosted by Washington University, June 16-20. Over two hundred participants from twenty three countries, including such distant points as Peking, Baghdad, Australia, and South Africa attended. Papers were presented on topics that included: all aspects of radiopharmaceutical design and preparation, relevant aspects of radionuclide research and methodology; problems arising from the use of radionuclides in biochemical and biological studies; and quality control problems relating to short-lived radiopharmaceuticals.

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ots nt Others from Mallinckrodt Institute working with Dr. Welch on the organizing committee were Diane Zaltsman, Secretary-Treasurer, Dr. M.M. Ter-Pogossian, and Dr. T.J. Tewson. In addition to the scientific lecture and poster sessions, the committee planned a social program for the participants and their families that acquainted them with the St. Louis area and provided them with a taste of its rich history.



The remarks of Dr. Welch bring smiles to the members of the Founding Committee of the Radiopharmaceutical Council at the Third International Symposium of Radiopharmaceutical Chemistry. Left to right are: D.J. Silvester, Ph.D.; A.P. Wolf, Ph.D.; G. Stöcklin, Ph.D.; M.J. Welch, Ph.D.; I. Cohen, Ph.D.; J.G. Cunningham, Ph.D., invited speaker; and T. Nozaki, Ph.D.



Dr. M. Maida, Visiting Professor in Radiation Sciences, right, and Dr. Kojima, Professor of Radiopharmaceutical Chemistry at Kyushu University, Fukuoka, Japan, enjoy a barbecue at Wohl Center.



Dr. Michael J. Welch escorts Bo-Li Liu, Associate Professor of Radiochemistry at Peking Normal University, Peking, China, and a participant in the Third International Symposium on Radiopharmaceutical Chemistry on a tour of his laboratory facilities at MIR.

INTERVENTIONAL RADIOLOGY at MIR

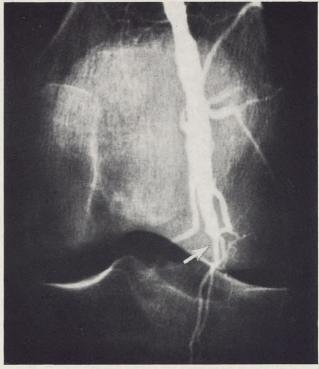
Mallinckrodt Institute radiologists are performing many new interventional radiologic procedures, some of which may replace surgery. Either alone or as an adjunct to a surgical procedure, many of these newer techniques offer the possibility of treating certain disease situations in less time and with less risk, discomfort, or cost to the patient. Angioplasty, Local Thrombolytic Therapy, Arterial Embolization, and Transhepatic Biliary Drainage are all non-surgical therapeutic procedures which are extensions of basic angiographic procedures in use for decades.

Angioplasty

Angioplasty, the balloon catheter method for opening atherosclerotic arteries blocked with plaque, is an extension of angiography, a procedure used to locate, identify, and measure arterial disease. The first balloon catheter for treating atherosclerotic peripheral vascular disease was introduced by Charles Dotter in 1964 and demonstrated the potential of the technique in treating arterial obstructions. In the mid-1970's, Dr. Andreas Grüntzig of Switzerland modified and refined the Dotter catheter by developing a balloon that could be inflated in a controlled fashion to a predetermined size. Grüntzig's modification was the breakthrough that has made percutaneous balloon angioplasty possible today.

In the last two years, Mallinckrodt radiologists Drs. Louis Gilula, Bruce McClennan, along with Drs. William Totty and Robert Stanley have performed over 60 peripheral and renal angioplasty procedures. Dr. Philip Ludbrooke anticipates the use of coronary angioplasty in the near future.

Dr. Gilula explained the diagnostic procedure: "The radiologist inserts a catheter into the femoral artery and, under fluoroscopic guidance, positions it near the site of the stenosis or blockage. Angioplasty is then performed to open the vessel." Dr. Gilula considers the ideal candidate for peripheral angioplasty as "one with peripheral vascular disease who experiences leg pain after walking less than one block, or has a non-healing foot or ankle ulcer." Dr. McClennan describes the ideal candidate for renal angioplasty as "someone with documented renal vascular hypertension caused by renal artery stenosis." "Angioplasty may be performed in older patients to preserve renal function," said Dr. McClennan.



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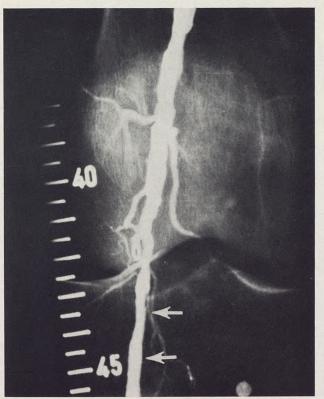
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Angiogram shows occlusion of popliteal artery with small collateral vessels filling the distal leg.

For angioplasty, the radiologist threads a catheter equipped with a balloon that will be inflated to a pre-determined controlled diameter when it reaches the blockage in order to compress the plaque and stretch the blood vessel to its former diameter. The balloon is then deflated and blood pressure is measured at the site to determine whether or not the newly created opening affords adequate blood flow; if not, the angioplasty procedure can be repeated. "The effect is usually evident immediately," said Dr. Gilula. "Patients with peripheral vascular disease experience relief of pain, may walk the next day, and are usually out of the hospital in three days." According to Dr. McClennan, renal vascular disease patients often show improved blood pressure on the treatment table and can be out of the hospital in two to four days. After treatment, continued small daily doses of aspirin help to offset any tendency to clot. In a study reported by Grüntzig et al, 87 percent of the patients with good initial treatment results have their treated artery still open after two or more years. If the condition recurs, the patient can be re-treated with either angioplasty or surgery.

Thrombolytic Therapy

Until recently, when angiography revealed that arterial obstruction was due to a clot or thrombus, treatment usually involved immediate surgical removal-a method not always technically feasible. Recently at Mallinckrodt Institute, Drs. Gilula, McClennan, and Totty have begun to treat selected patients with a new local intravascular method of Thrombolytic Therapy. Dr. Totty explained, "This method involves placing a catheter into the blocked artery. With the catheter tip just above or into the thrombus, very small amounts of a clot dissolving drug (streptokinase or urokinase) are directly infused. By using small amounts of the drug many of the problems associated with generalized intravenous treatment can be avoided. Several patients have now been successfully treated, including one patient with a totally blocked distal aorta."



After a 24-hour streptokinase infusion, the vessel has opened and the area of narrowing is again seen. An angioplasty was subsequently performed. The patient is now doing well after four months.

Transcatheter Arterial Embolization

Since 1975, using an interventional method called Transcatheter Arterial Embolization, Dr. Robert Stanley and Dr. William Murphy have collaborated on the therapeutic treatment of over a dozen patients with a variety of soft tissue malformations ranging from lesions in the pelvis to lesions in the tip of the finger. The malformations, clusters of abnormal vessels developed into a communication between an artery and a vein, are unusual lesions that sometimes behave like tumors, but are actually benign nontumorous entities. "They are usually congenital in origin or develop following penetrating trauma such as a gunshot wound," said Dr. Stanley. "After diagnosis by arteriography, we place a catheter directly into the feeding vessels, then inject minute particles of thrombogenic material into the bed of the arteriovenous malformation to obliterate the vascular spaces. The embolization agent we prefer to use today is a polyvinyl alcohol sponge which remains within the body and permanently obliterates the abnormal vascular tumor bed."

These arteriovenous malformations are present in growing children and the long term effect of treatment can only be assessed over a period of years. For example, excessive growth of a leg may be associated with the presence of soft tissue vascular malformation. In order to determine whether or not the embolization procedure has adequately reduced the malformation, subsequent growth of the legs must be monitored carefully until the child's normal growth period is completed.

Dr. Murphy added, "In the majority of cases we have treated, the results have been most gratifying. Large, deforming, and sometimes intermittently bleeding lesions have been well controlled for a period of several years, eliminating the need for radical surgery. We are currently following six patients in various stages of this embolization therapy program who are being treated for a variety of lesions." With the results already evident, Dr. Stanley and Dr. Murphy feel that the technique of transcatheter embolization of large chronic arteriovenous malformations in the trunk and limbs should be given consideration as the primary form of treatment when the dominant arterial feeder(s) can be clearly identified and subselectively catheterized. This technique offers the potential for sparing the patient extensive surgery.

INTERVENTIONAL RADIOLOGY

Dr. Mokhtar Gado, Mallinckrodt neuroradiologist, has utilized embolization techniques since 1971 to treat vascular malformations supplied by intracranial blood vessels, vessels of the head and neck, and tumors in the region of the pharynx, paranasal sinuses, tongue, face, or neck.

He explained, "The technique depends upon the high blood flow in the abnormal vessels causing the emboli to lodge in them rather than in normal vessels. Therefore, more and more of the abnormal vessels are obliterated during the procedure." Dr. Gado expects new developments in this area to broaden the application of current procedures.

Transhepatic Biliary Drainage

Percutaneous Transhepatic Biliary Drainage is an interventional technique Dr. Philip Weyman has used to restore bile drainage in patients whose bile flow is inhibited by unresectable biliary obstruction, such as pancreatic cancer, metastatic disease, cancer of the biliary duct, or surgically unapproachable benign structures. The percutaneous procedure, performed under local anesthetic, involves threading a multiholed catheter into the liver. The radiologist attempts to lace the catheter through the blockage and establish internal bile drainage to the duodenum. If the obstruction is impenetrable, the catheter establishes a channel to drain bile externally. The patient can usually be discharged in a week to ten days.

Dr. Weyman stresses that while surgery is still the primary corrective treatment, the percutaneous drainage is a desirable palliative procedure to restore bile drainage and alleviate the affects of restricted bile flow. Occasionally radiologists establish transhepatic biliary drainage to improve the patient's condition preparatory to corrective surgery. In five months, Dr. Weyman has installed two external and three internal biliary drainage catheters.

Whether these various interventional procedures serve as complements to surgery, options to surgery, or as potential primary treatment methods, they continue to widen the scope of patient treatment at the Mallinckrodt Institute of Radiology.

New Computer Technique Expedites Patient Service

In the present age there seems to be a computer for almost everything—from checking out groceries to doing library research. At Mallinckrodt Institute, computers play a powerful role in enhancing the quality of patient care and making the operation of the Institute more efficient and more productive.

The Diagnostic Computer Section, under the direction of Dr. Gilbert Jost and Rex Hill, M.S., is making a dramatic contribution to patient care through the use of optical reading techniques to track the points of each patient's progress through the Institute-from moment of arrival to moment of departure. "The technique, which is similar to the one used in food markets, is reliable, accurate, and quick to do," said Dr. Jost. A floor receptionist first logs the patient arrival time in the computer terminal by passing a computer wand over the x-ray requisition number. After the x-ray has been taken, the technologist registers completion time in a second terminal and sends the film to the quality control technologist, who, after approving film study quality, registers finish time in a third terminal. The receptionist then registers patient departure time in the computer.

In order to provide a complete record of the patient's visit to the radiology department, the times

of the following additional events are captured:

1. When old films are matched with new and made available for reading by the radiologist.

2. When films have been read and can be returned to the film library.

3. When the radiologist's dictation is transcribed, the report signed and made available for distribution.

According to Mr. Hill, statistics will be drawn from data accumulated on a continuing basis over a period of time. These statistics will aid in defining patterns and isolating problem areas. In addition, current information will be available on terminals at floor supervisors' desks. With pertinent data available and the names of patients who have waited over 30 minutes on display, supervisors will be better able to direct attention to delays and schedule problems as they occur. This data will also be available at inquiry stations in the department. For example, a physician coming to the MIR film library area can be accurately informed of the status of a patient currently undergoing an examination.

"This application of a bar code technique is unique to Mallinckrodt," says Dr. Jost, "but it should prove to be a useful method for serving patients faster and more efficiently."

China Officials Visit Mallinckrodt



"Everywhere we go we are met with smiling faces," Wang Chubin, head of the six-member delegation from the People's Republic of China, said through their interpreter on a recent visit to Mallinckrodt. This first official visit was part of a St. Louis-Nanjing (Nanking) "sister city" relationship which was established in October, 1979, and is the nation's first such relationship with a Mainland Chinese city.

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Dr. Lewis J. Thomas, Jr., Director of the Washington University Computer Laboratory, was in charge of the tour which included activities at the medical center relevant to the interests of the group. Dr. Barry Siegel hosted a tour of Nuclear Medicine Facilities and Dr. Michel Ter-Pogossian demonstrated the PETT VI (positron emission transaxial tomograph) in the Division of Radiation Sciences. The PETT VI is the first in the PETT series to use cesium fluoride crystals as detectors, making it the fastest such detection system in the world for providing striking views into the living human brain.

Zhou Bofan, a vice-chairman of the Nanjing Municipal Revolutionary Committee said that he was most impressed by the modern diagnostic equipment such as the PETT and the CAT Scanner at Mallinckrodt Institute. Dr. Michel Ter-Pogossian, far right, is pictured at the PETT VI with three members of the Nanking delegation; translators, Shirley Cheng and Jing-Shiang Cheng of the Biomedical Computer Laboratory; Dr. Lewis J. Thomas, back left; and Mr. Edmund Greene, back right, of the Sister-City Committee.



Dr. Barry Siegel describes activities within Nuclear Medicine to the visiting group and Mr. Frank Murphy of Mallinckrodt, Inc.



MEDICAL LIBRARY

Residents' Farewell On the evening of June 23, the Washington University Alumni Club was the scene of a convivial gathering of MIR staff members and residents and their spouses to celebrate the completed residency training of Drs. Baron, AufderHeide, Bishop, Brinkley, Howard Glazer, Monsees, Oakley, and Totty, and the year's fellowship of Dr. Balfe. Following cocktails and hors d'oeuvres in the main lounge, the 90 guests were seated in the spacious dining room overlooking the Arch and the St. Louis riverfront. Dr. David Hardy, Chief-Resident, 1980-81, presided and Dr. Ronald Evens, after congratulatory remarks, presented each honoree with a commemorative brass plaque.

Foreign Lectures

Dr. Robert Stanley presented four lectures at the 5th International Meeting on Body CT in Rome, Italy, during May 19-23.

Dr. James E. Marks was invited as a guest lecturer from the United States to the Third European Clinac Users Meeting held in the radiation center of Aalborg, Denmark on May 8-9. He spoke on "The Use of High Energy X-rays to Spare Normal Brain, Cranium and Soft Tissues" and "The Use of Electrons to Spare the Opposite Parotid for Selected Head and Neck Cancers."

Awards

Dr. Todd H. Wasserman, Assistant Professor of Radiology in the Division of Radiation Oncology, has been awarded a first-year Junior Faculty Clinical Fellowship of the American Cancer Society for the period July 1, 1980 - June 30, 1981.

Dr. Joseph R. Simpson is a second-year recipient and Dr. Hywel Madoc-Jones has been awarded the fellowship for the third year.

Panel Member

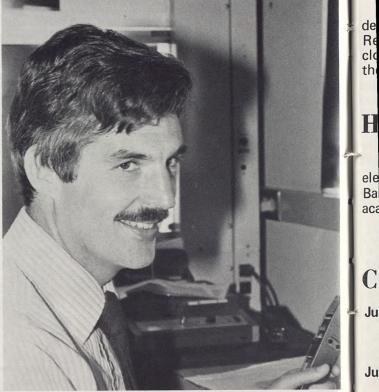
Dr. G. Leland Melson discussed several aspects of residency training program as a panel member considering Post Graduate Year-1 Options at the Annual Meeting of the Association of University Radiologists in Tucson, March 26.

On May 19, Dr. Melson participated in a panel "Clinical Value of Ultrasonography in Urological Evaluation" where he discussed the relationship of ultrasound to other imaging techniques at the Annual Meeting of the American Urological Association in San Francisco.

Scientific Exhibit

Dr. Carlos A. Perez presented a scientific exhibit on "Cancer Therapy by Hyperthermia, Drugs, and Radiation" at the Third International Symposium, held at Colorado State University in Fort Collins, Colorado.





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Dr. John Forrest ('71), Chief of Diagnostic Radiology at the University Hospital, UCSD, was a Visiting Professor in Chest Radiology, June 23-27. Dr. Forrest was Associate Professor of Radiology at Mallinckrodt until 1977.

Dr. Bruce McClennan was a Visiting Professor at the University of Iowa April 28-29.

Dr. Robert Stanley addressed the Greater Kansas No City Radiological Society and was a Visiting Professor at the University of Kansas Medical Center and St Luke's Hospital in Kansas City on April 16 and 17.



Chief Residents

Dr. David Hardy has been appointed Chief Resident for 1980-1981 and Dr. Harvey Glazer, Co-Chief Resident. Drs. Hardy and Glazer will be working closely with Dr. Ronald Evens and Dr. Lee Melson in the operation of the MIR residency training.

Honored

Dr. Jill White, second year resident, has been elected the MIR Housestaff Representative to the Barnes Hospital Advisory Committee for the 1980 academic year.

CALENDAR OF EVENTS

July 11-17, 1980

ÁMERICAN SOCIETY OF RADIOLOGIC TECHNOLOGISTS Atlanta, Georgia

July 13-19, 1980

NATIONAL RADIOLOGIC TECHNOLOGY WEEK

July 20-24, 1980

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AMERICAN MEDICAL ASSOCIATION Chicago, Illinois

September 21-25, 1980 AMERICAN COLLEGE OF RADIOLOGY New Orleans, Louisiana

October 21-25, 1980 AMERICAN SOCIETY OF THERAPEUTIC RADIOLOGISTS Dallas, Texas

November 16-21, 1980 RADIOLOGICAL SOCIETY OF NORTH AMERICA Dallas, Texas

Lectures - Symposiums

Recent talks by Dr. Carlos A. Perez include:

"Organization of Radiation Oncology in the Cooperative Groups," Clinical Cancer Investigation Review Committee, NIH, Bethesda, Maryland.

"Frontiers of Cancer Research," at the First Community Conference on Cancer Nursing in Ft. Worth.

"Carcinoma of the Prostate," Southwestern Medical School, Dallas.

"Cancer of the Uterine Cervix" and "Cancer of the Prostate," Allegheny General Hospital, Pittsburgh.

Dr. Robert Stanley was a member of the faculty for an Imaging Seminar at the Hospital of the University of Pennsylvania, Philadelphia, April 9-11.

Dr. James E. Marks was a member of the faculty at a workshop sponsored by the University of North Carolina School of Medicine, March 14, in Chapel Hill, on Radiotherapy of Primary Malignant Gliomas. He spoke on "Review of Studies of Radiotherapy of Malignant Gliomas" and "Mechanisms of Evaluation of Response to Therapy."

Dr. Patrick R. M. Thomas presented a talk on "Prospective Film Review in a Clinical Trial Involving Radiotherapy," at the American Society of Clinical Oncology, May 27, in San Diego.

Dr. Robert Stanley addressed the American Association of Anatomists in Omaha on April 30 during a forum in applied anatomy.

Dr. Carlos A. Perez presented three lectures as a member of the faculty for a refresher course sponsored by the University of Minnesota in Minneapolis, May 21-23. His subjects were:

- (1) Current Clinical Status of Hyperthermia,
- (2) Periaortic radiation and Prostate Cancer, and
- (3) Irradiation of Lung Cancer Techniques and Results.

Dr. Barbara B. Sterkel presented "Persistent Renal Activity Seen in Gallium Scans in Patients with Severe Hepatocellular Disease" at the 27th annual meeting of the Society of Nuclear Medicine, June 24-27 in Detroit.

Dr. Carlos A. Perez presented "Medical Aspects of Treatment Planning in Lung Cancer" at the American Association of Physicists in Medicine, July 28, in Minneapolis.

Cancer Workshop



Drs. Theodore Phillips (left) and Todd Wasserman (right), speakers at the May 1 Cancer Workshop, with Dr. Carlos Perez, Director of the Division of Radiation Oncology.

At a recent Cancer Workshop, sponsored by the Division of Radiation Oncology of the Mallinckrodt Institute of Radiology, the subject of radiosensitizers and protector agents in cancer therapy was discussed by Dr. Todd H. Wasserman, Assistant Professor, Division of Radiation Oncology and Dr. Theodore L. Phillips, Professor and Chairman, Department of Radiation Oncology, University of California Medical Center, San Francisco. Dr. Wasserman, who worked with Dr. Phillips for three years prior to coming to St. Louis to join the staff of Mallinckrodt, was awarded the 1978 Resident Essay Award of the American Society of Therapeutic Radiology for his work with radiosensitizers. The subject of the workshop was the use of drugs that have no direct effect on cancer but modify the effect of ionizing radiation on cancer.

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Currently being investigated are two classes of drugs. The first type, those which sensitize tumor cells to radiation but do not sensitize normal tissues increase the selective ability of radiation to kill cancer cells without increasing the toxicity of radiation. Laboratory studies began on these drugs in the mid 1970's and clinical trials in the United States began with a drug called Misonidazole in 1977. Conducted primarily through the Radiation Therapy Oncology Group, the trials were initially done at the University of California at San Francisco and are now being conducted at Washington University by the Division of Radiation Oncology. The sensitizers work by increasing the killing potential of radiation on cancer cells. Early clinical trials with Misonidazole on several hundred patients have offered promising results, although there are limitations of its use because of some drug related side effects on the nervous system. There is an increasing effort by chemists and pharmacologists to develop other analogs of this drug which would lack the neurotoxicity. Currently there are nine active clinical Phase II trials involving Misonidazole underway in the United States and other trials underway in England, Canada, and other countries. Preliminary data suggests that despite the drug related toxicity, it can be given with high degree of safety provided the total drug dose is limited. There is a suggestion that the use of the drug in conjunction with radiation increases cancer control of some tumors.

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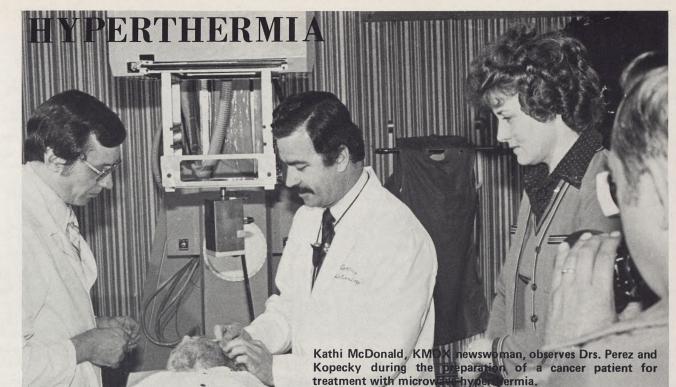
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The second area of new research in cancer therapy involves the use of drugs that protect the normal tissues from radiation without protecting the tumor. A series of compounds was originally developed by the Army at Walter Reed in Washington, D.C. in an attempt to protect troops from the threat of radiation sickness. The compounds did not perform as expected, but were discovered to protect normal tissues selectively against the effects of low dose radiation. As a follow-up of extensive laboratory work on one of these drugs, called WR-2721, and its protective effects against the bone marrow toxicity of chemotherapy agents, Drs. Phillips and Wasserman will participate in the first clinical trial of this drug in, the United States sometime in the summer of 1980.

The clinical staff of the Division of Radiation Oncology will be seeking participation of patients and referring physicians in the ongoing clinical trials of both the radiosensitizers and the radioprotectors.

Dr. Phillips and Dr. Wasserman, who currently have authored several papers on the subject of their research, are advisors to the National Cancer Institute for development of further research in this area. They were recently featured at a meeting organized as a conference on radiation sensitizers and protectors, held in Key Biscayne, Florida.



Hyperthermia, high body temperature induced for therapeutic purposes, was first documented in 1866 as effecting tumor regression, yet only in recent years with the development of new technology, has it become a viable treatment modality. Whether induced by hot water baths, ultra-sound waves, low radiofrequency waves, microwaves, heated blood perfusions, or delivery of heated anesthetic gases to the lungs, hyperthermia temperatures of 107.6° to 113° tend to kill cancer cells but leave normal cells less affected. Cancer cells are more susceptible to heat because of their proliferating nature, poor circulation, poor nutrition, and characteristic inability to cool. In addition, cancer cells appear to be less able to repair from treatment by conventional methods if they are combined with hyperthermia. Radiotherapy, for example, is 40% to 60% more effective when combined with hyperthermia.

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In a recent television interview in the Division of Radiation Oncology of Mallinckrodt Institute, Dr. Carlos Perez, Director, Dr. Walter Kopecky, and one of their patients, Mr. Robert Siemer, discussed the procedure during an actual treatment session. Mr. Siemer, who was being treated for cancer with microwave hyperthermia following a complete series of radiotherapy treatments, said he experienced only mild discomfort, initially from the insertion of probes, then from the five-minute period of heat rise, and finally from the ninety-minute duration of treatment.

To begin the procedure, Dr. Perez inserted one of two small probes into the tumor core; the other, into superficial normal tissue. He explained that the probes are inserted without anesthetic because probe insertion is no more painful than anesthetic injection. Then, while the microwave transmitter was being aligned with the tumor and the controls were being set, Mr. Siemer described his treatment, "Other than an occasional mild burn and the discomfort of lying on a hard surface, I have found the procedure to be nearly painless." Dr. Kopecky, indicating dials on the monitor, added, "The gauges show the temperature being measured by the probes, but Bob alerts me if any particularly strong heat sensation occurs." Having nearly completed the hyperthermia treatment series, Bob Siemer spoke from experience, "I usually just relax and take a little nap."

Microwave hyperthermia treatments are performed at Mallinckrodt Institute more frequently than at most other hospitals in the country, and approximately 80% of the patients treated here in the last two years have experienced significant tumor reductions. Dr. Perez stressed, however, that reduction does not translate to cure. "The procedure is still in the investigative stage, with only the potential for cure."

New Technique To Help Predict Patient Response To Endocrine Therapy

Hormone therapy has long been a treatment option for certain types of cancer but, until recently, its track record has been less than impressive-only one patient in three has benefited from hormonal manipulation. This statistic is due not to any major shortcoming of hormonal therapy itself, but rather to the inability of physicians to predict which tumors will respond to this kind of management. Even after recent work which increased the response in breast cancer patients to between 50% to 60%, there was still a glaring need for a more reliable way to predict a tumor's hormone-responsiveness. Now, B.R. Rao, Ph.D., Mallinckrodt Institute Section of Cancer Biology, and his co-workers have given good reason for optimism regarding uncertain future of hormone therapy. Dr. Rao's new technique for detecting hormone receptors may well be the key to predicting accurately which tumors will respond to hormonal manipulation.

The rationale behind hormone therapy is relatively simple. In certain normal cells, steroid hormones are essential for normal cell growth and protein synthesis. When cells undergo the transformation from normalcy to malignancy, they may or may not retain this hormone dependency; if they do remain hormonedependent, "ablative" hormone therapy (i.e., deprivation of necessary hormones) will interfere with their growth and eventually lead to tumor regression.

One way of determining whether a tumor cell is hormone-dependent is to check for the presence of "hormone receptors" in its cytoplasm. This is more easily said than done, for current methods have been time-consuming and have yielded unacceptably high numbers of false-positive and false-negative cases.

Dr. Rao and his associates have developed a technique which promises to simplify the identification of hormone-responsive tumors and improve the reliability of previous assay procedures. He uses fluorescein to label sex steroid hormones (specifically, estrogen and progesterone). These labeled hormones are incubated with a tumor tissue sample, and count the number of cells to which they bind.

This technique eliminates some of the technical impasse which has previously impeded the prediction of the response of tumor-to-hormone therapy. Much remains to be done, however. Investigators must closely follow those patients whom the assay has singled out as prime candidates for hormone therapy; such studies will reveal how closely the assay's prediction correlates with the patient's response to endocrine therapy. Also, using the Division's new flow cytometry facility (provided by contributions of the Advertising Federation of St. Louis), Dr. Rao and his associates will refine their procedures for quantifying the fluorescence and for counting the cells to which hormones will bind. If Dr. Rao's technique is as effective as it appears to be, it may contribute significantly to the treatment of breast, prostate, uterine, and renal cancers.

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RESIDENTS, FELLOWS & TRAINEES 1979-1980



Back row, left: Drs. Balfe, Ling, Thaler, Totty, Brinkley, Scales, Vannier, Stein, Johnston, Bauer, Machefsky, Glazer, Chandra-Sekar. Center row: Drs. Yu, Glazer, Lenobel, Spies, Engelstad, AufderHeide, Bishop, Nicol, Miller, Monsees, Odrezin, White. Front row: Drs. Cintron; McDonald; Hardy; Sterkel; Melson; Baron, Chief Resident; Evens, Radiologist-in-Chief and Director of MIR; Oakley, Co-Chief Resident; Palmer; Kopen; Reed; Wahl.

Monte Carlo Seminar



A view of Monte Carlo harbor.

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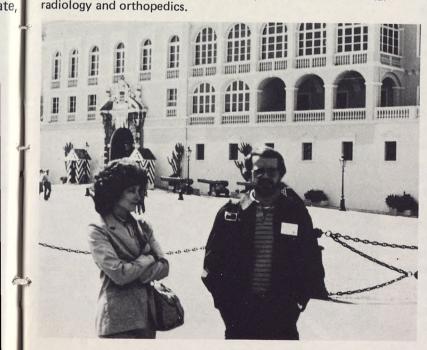
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The second annual continuing medical education program, sponsored by the Mallinckrodt Institute of Radiology under the direction of Drs. Louis Gilula and William Murphy was held at the Loews Monte-Carlo hotel complex on the French Riviera, May 3-12. Dr. William McAlister was also a member of the faculty of distinguished American and European physicians who presented current concepts in musculoskeletal radiology and orthopedics.





Dr. William Murphy spoke on "Forearm and Hand Arteriography" to the 125 participants.



Following the symposium, Dr. Emily Smith visited Florence and Rome, Italy. Here she stands by the majestic doors to the Church of Santa Croce (Sacred Cross) in Florence.

Dr. and Mrs. Charles Hobby of Valdosta, GA visit the Royal Palace of Prince Ranier and Princess Grace of Monaco.

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Addresses Top Radiologic

Technology Meeting



Glenn P. Glasgow, Ph.D., Assistant Professor in Radiation at Mallinckrodt Institute of Radiology and Washington University, spoke on "Quality Assurance in Radiation Therapy" at the 52nd Annual Meeting of The American Society of Radiologic Technologists, July 11-17, in Atlanta.

Dr. Glasgow joined the staff at Mallinckrodt Institute in 1974 as a Post-Doctoral Fellow. In 1975 he became an instructor in Radiation Physics in Radiology, eventually moving to his present Assistant Professor post. He will be one of the 38 important health care professionals invited to address this scientific gathering of over 3,000 radiologic technologists.

The ASRT Atlanta Annual Meeting will provide educational opportunity to diagnostic radiographers, radiation therapy technologists, nuclear medicine technologists, and diagnostic medical sonography technologists from across the United States.

Also offered at this professional gathering will be scientific displays, 32 symposia and seminars, and over 100 commercial exhibits.

Dr. Barry A. Siegel presented a talk on "Radionuclide Renal Studies" at the annual meeting of the Technologists' Section of the Society of Nuclear Medicine, February 6-8, in Louisville, Kentucky. Deborah Christensen, C.N.M.T., was awarded first prize in the Scientific Papers Division for her presentation, "A Technique for Performing Simultaneous Ventilation-Perfusion Studies Utilizing Kr-8/M gas and Tc-99m MAA."

Authors Nuclear X-ray Atlas

Radionuclide Imaging Artifacts, an atlas of nuclear x-ray images compiled by **Donald R. Bernier**, C.N.M.T., of the Nuclear Medicine Division of Mallinckrodt Institute of Radiology and L. David Wells, C.N.M.T., of the Nuclear Medicine Division at University Community Hospital in Tampa, illustrates unusual problems associated with radionuclide imaging. The authors intend for the book to serve as both an educational document and a practical reference tool when technical problems occur. They hope that sharing these images will result in an overall improvement in quality control and in the quality of nuclear medicine practice.

Norman Hente, R.T., lectured on "Preparing Scientific Exhibits" at the March meeting of the 7th District (Therapy) MSRT. He also spoke on "Photography in a Radiology Department" at the Gateway Chapter regional meeting of the Biological Photographers Association held at MIR on March 22.

Opposite page

Barbara Hente demonstrates her technique of chest compression on "Resusci-Annie" while Norm Hente practices rescue breathing. This special recording mannequin records how much air is being blown into the victim's lungs and beeps if the student's hands are placed at a spot on the chest that would cause a cracked rib. Lights flash to indicate too much pressure applied.

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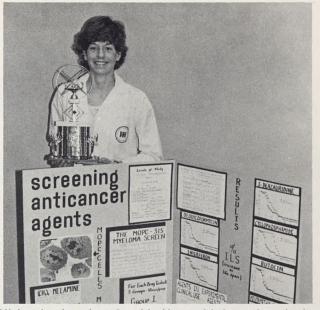
CPR Workshop at MIR

Eleven MIR employees were among 28 members of the 4th District of the Missouri Society of Radiologic Technologists who participated in a two-day workshop in April leading to certification in CPR (cardiopulmonary resuscitation) by the St. Louis Heart Association. Linda Kratz, R.N., of the MIR nursing staff was one of six certified instructors. The seminar (7 E.C.E. points) included a slide lecture, movie, practical demonstrations, and hands-on experience.

The training combines a procedure of chest compression and mouth-to-mouth breathing to keep blood and oxygen flowing through the body until the victim can receive more sophisticated cardiac care in an ambulance or hospital.



Top Honors

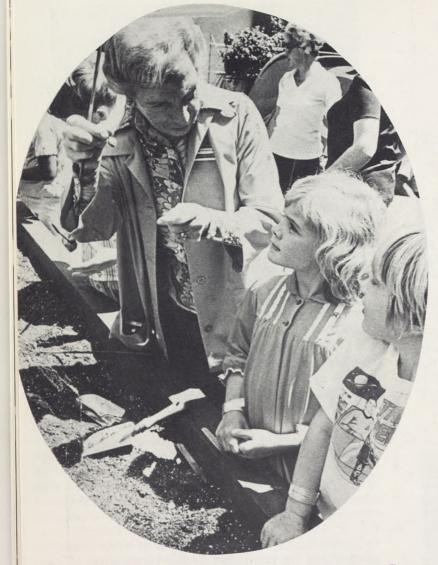


High school senior, Cynthia Hegg with her prize-winning myeloma exhibit.

Cynthia A. Hegg, a senior at Parkway West High School in St. Louis County, received top honors at the 1980 Monsanto/Post Dispatch Greater St. Louis Science Fair, for her research into the effects of a number of anticancer agents on a murine myeloma that closely parallels human multiple myeloma. During five months of collaborative work with Mr. Dean Coulter in the laboratory of Dr. Fred Valeriote in the MIR Section of Cancer Biology she compared lifespans of treated tumor-bearing mice with those of untreated controls, while simultaneously measuring the toxicity of the drug dosages in normal mice. Protocols based on positive results of these and other studies will be developed at the Washington University Medical Center over the next few years.

Cynthia's exhibit, on display at the Museum of Science until Spring, 1981, reflects the analytical thought, scientific content, and research excellence stressed by the awarding institutions. Among her awards were a \$4000 scholarship from Monsanto, the Curator's Scholarship for Tuition and Fees from the University of Missouri, and a \$200 scholarship from the Medical Society of Greater St. Louis. In addition, Cynthia received the Blue Award in the Honors Division of the Science Fair and certificates of achievement from the American Cancer Society and the United States Air Force.

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In her nature classes at St. Louis Children's Hospital, Dorothy Evans combined her love of gardening with her love of the young patients.

"She Had Magic..."

I met Dorothy Evans only a few months ago, when she was a patient in the Division of Radiation Oncology at Mallinckrodt Institute. I found myself thinking about her a great deal. There was some special quality about her-a certain zest for life and loving in her eyes-that had touched my heart and my imagination. I saw her in the midst of young professional women from the hospital staff, laughing mischievously, her eyes sparkling with good humor and warmth; I saw her talk about her "greenhouse" project at St. Louis Children's Hospital with the affection of a parent; I saw her look at John, her husband of 39 years, with real devotion and understanding. I saw her radiantly happy as she visited with her son, John who was to receive his Ph.D. in Public Health from Harvard University in late spring; I saw her interest quicken as someone mentioned one of her many friends, whether it be her daily walking partner (3 to 5 miles each morning), a devoted neighbor, or a long-time associate with volunteers at Missouri Botanical Garden. I also saw Dorothy sleeping in a hospital bed, her husband sitting quietly beside her, and hovering in the ceiling a brightly colored enormous helium balloon bedecked with multi-colored ribbons and bearing the greeting, "Happy Easter." Dorothy died of multiple myeloma on April 21, 1980.

Three years before her death, Dorothy played a fast game of tennis four times a week, walked 13 miles to the Arch from her home in Kirkwood, and during her 12 years as a Volunteer Nature Therapist at St. Louis Children's Hospital, Dorothy touched the lives of many young patients, combining in one project her love of nature and gardening with her love of children.

In the beginning, Dorothy had only a few plants to use in her classes, and so each Sunday, she gathered

rPatients"

plants and wild flowers for the hospital-bound children from the Evans' farm in St. Francois County. Through the years, as a result of her tireless efforts and in spite of setbacks caused by lack of space, her project grew from a modest roof-top vegetable garden to a real greenhouse in which to hold her classes. Construction was done by John Evans and his neighbors and associates; Huntleigh Hills Garden Club contributed time and money; Dorothy's Alumnae Club of Stephens' College provided the sink; and unding came from grateful parents of hospitalized pungsters. The greenhouse, dedicated in November 179, was the story of love, labor, and determination n the part of one Dorothy Evans—indeed, a dream nat came true.

Three years ago, Dorothy experienced severe rib pain during a tennis game—the first indication of nultiple myeloma, a bone marrow malignancy. In his disease the malignant plasma cells in the bone arrow cause many areas of bone to be resorbed, ading to soft and fragile bones and a high incidence pathologic fractures.

In her valiant fight against cancer, Dorothy underwent a program of chemotherapy and spinal surgery, and multiple courses of radiotherapy in the Division of Radiation Oncology at Mallinckrodt Institute of Radiology. Even after suffering a loss of hearing from 1 tumor in the nerve center at the base of the skull, Dorothy continued to conduct her weekly classes at Children's Hospital until December 1979.

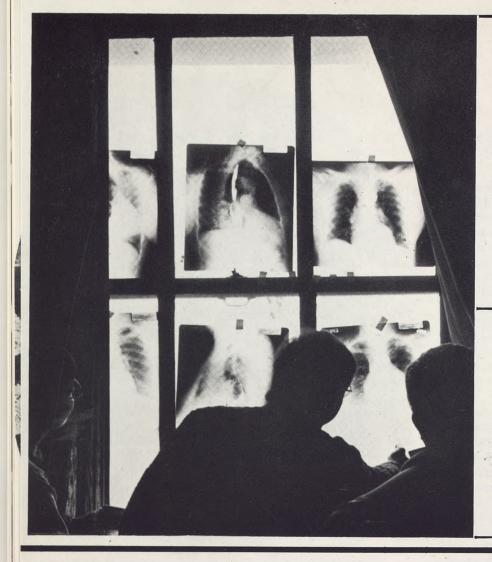
Just as during the years Dorothy provided therapy to many children through her patience, love, and knowledge of plant and gardening, the example of her own life of courage and determination became therapy to people around her, inspiring others to be brave and strong. We are grateful for having known her.

"Word Of Comfort"



Fred Bingaman with Joy Van Dyke awaiting an X-ray on the fifth floor of Mallinckrodt.

"Most children like grandfathers," says Fred Bingaman, a 77-year-old grandfather, who has been a St. Louis Children's Hospital volunteer transporting children for pediatric X-ray at Mallinckrodt for four years. He feels that the "grandfather image" helps him in what he considers the most important aspect of his job-comforting and reassuring frightened children. The measure of Mr. Bingaman's success is reflected in the smiling faces of the children.





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Virginia Trent Director and Editor

Kay Porter Assistant Editor

Norman Hente Tom Murry Photographers

"Teaching Goes Or

During a spring power failure at the Medi Center, Dr. Robert C. McKnight showed ingenu persistence, and dedication as he utilized nearest available window light for reviewing diovascular films with radiology residents, Floyd Scales, left, and Michael Vannier, cer (Photo by Dr. William Totty)

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