Pharmaceutical Manufacturers Association Foundation, Inc.

1982 Annual Report

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Applications (inside back cover)

A Response

In 1981, the PMA Foundation noted that every effort would be made to increase its financial resources, given the increasing number of individuals in the academic community seeking financial assistance from the private sector. There is no question that the pharmaceutical industry has a most vital interest in maintaining and increasing the number of scientists and physicians who participate in the development of the basic knowledge on which drug discovery and development depends. The Foundation is one way that the industry is meeting this responsibility.

A major effort was initiated this year to increase the funds available to the PMA Foundation. The early response has been most encouraging. The PMA Foundation Board of Directors believes that over the 1983-85 period, the Foundation will enjoy a significant increase in funds. As a consequence, the Foundation will be able to improve its current programs and will be able to expand into new areas of support.

The PMA Foundation has continued during the year to be responsive to the needs of the groups of academic scientists towards which its programs are directed. The Board of Directors extended the number of awards this year beyond program budgets in recognition of the number of well-trained scientists who applied for support. While the numbers of awards are still relatively small under all of the programs offered by the Foundation, the accumulation of the number of awardees over time is such that a significant impact is apparent. For example, through the Foundation's research starter grants program and faculty awards in pharmacology, about 20% of all full time pharmacology faculty in the United States have been or are being supported by the Foundation.

The pharmacological sciences have expanded substantially in the last two decades. It is this very success which now makes them especially vulnerable to budgetary reductions. Large sums are needed just to maintain the efforts in training and research which have kindled the remarkable discoveries in the field. Smaller budgets for training and research in the pharmacological sciences result in shortages of scientists and physicians who participate in the discovery and development of new drugs. The PMA Foundation's programs are aimed at helping, in part, some of these scientists and physicians. The Foundation looks forward in the coming years to assisting even more individuals as its financial resources increase.

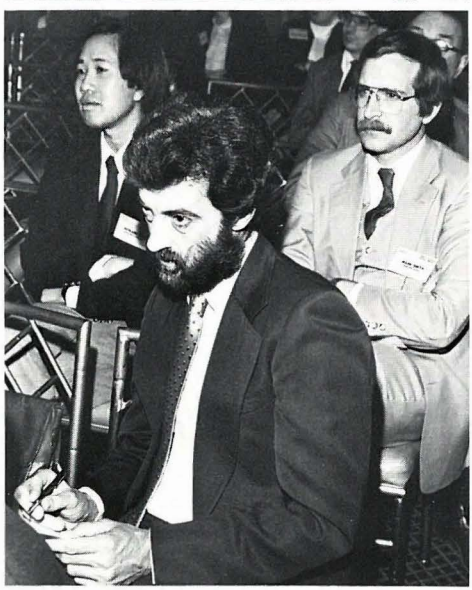
A SENSE OF CAMARADERIE

A meeting of the Foundation awardees was held in December. An excellent keynote address at the general session set the tone for the meeting. Dr. Sidney Pestka, Full Member and Head of the Laboratory of Molecular Genetics, Roche Institute of Molecular Biology, spoke on "The Human Interferons: Purification, Cloning, Production in Bacteria and Pharmacology". Mr. Irwin Lerner, Chairman of the PMA Foundation Board of Directors, welcomed the awardees and committee members and gave an update on awards for 1983 which had been authorized the prior day. The general session concluded in mid-morning to enable the various subgroups of awardees to convene in special sessions to hear papers from current and past awardees.

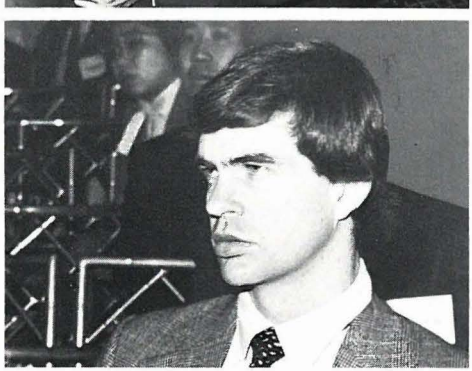
In the afternoon, the three groups again met separately. The clinical pharmacologist subgroup heard Dr. David G. Shand, Professor, Division of Clinical Pharmacology, Duke University, speak on "Experimental Design in Clinical Pharmacology". The pharmacology-morphology subgroup devoted the afternoon to a poster session. The basic pharmacology subgroup heard a presentation by Dr. Frank G. Standaert, Professor and Chairman, Department of Pharmacology, George-

town University on the future of pharmacology.

In August, 1982, a meeting was held with the research starter grantees and the advanced predoctoral fellows in pharmacology and toxicology during the fall meeting of the American Society for Pharmacology and Experimental Therapeutics. The speaker was Dr. Thomas Tobin, Professor of Veterinary Science and Toxicology, University of Kentucky, who spoke on "Drugs and Analytical Chemistry: Their Influence on Horse Racing".



These meetings continue to provide opportunities for the advisory committee members to gain perspectives on how well the various programs are achieving their goals. For the awardees, the meetings provide unique opportunities for exchange of information in an informal atmosphere. Many of the awardees have indicated that this characteristic is a big 'plus' of the meeting. A common comment is that the meetings foster a real sense of camaraderie among the awardees.



ACTIVITIES

Since its formation in 1965, approximately $13.5 million has been authorized by the PMA Foundation for a variety of workshops, conferences, research projects and educational programs. Of this amount, approximately $3.8 million has been used to support research and more than $9.0 million has gone into educational awards. The remaining $500,000 has provided financial assistance for scientific meetings, along with a small portion for publications.

Virtually all of the 1982 grants and awards were made within programs sponsored by the Foundation. These include three faculty level programs of salary and fringe benefit support, four fellowship programs—two postdoctoral, one at the advanced predoctoral level and one at the medical student level—plus a program of research starter grants for beginning investigators wishing to move into areas of independent research. An award to assist in expediting the research efforts of new clinical pharmacology units or those with new directors is also available.

Through these programs in 1982 the Foundation assisted an additional 58 individuals. All of these individuals were helped at a crucial time in their professional development. The Foundation has, in its slightly more than seventeen years of existence, helped more than 750 individuals through its research and educational support programs.

EDUCATION AND TRAINING PROGRAMS

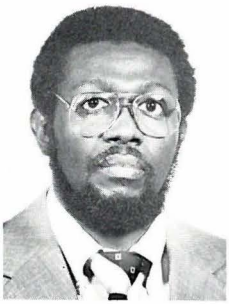
To further its objectives in the field of education, the PMA Foundation sponsors four programs in clinical pharmacology: one in the combined field of pharmacology-morphology, one in pharmacology or toxicology, one in basic pharmacology and one in toxicologic pathology.

CLINICAL PHARMACOLOGY
Faculty Awards in Clinical Pharmacology

The four clinical pharmacology programs provide opportunities at the student, fellow and faculty levels. Through the Faculty Development Awards in Clinical Pharmacology program, the Foundation makes two-year awards to medical schools for salary and fringe benefits support of full-time junior faculty members. The Foundation has set a ceiling of $30,000 on the amount of its participation in total yearly salary and fringe benefits for any candidate.

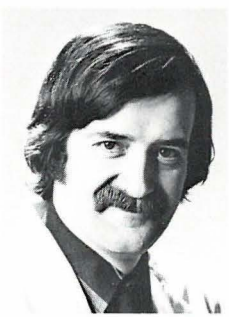
With the awards scheduled to begin July 1, 1983, 63 individuals have been supported under this program since 1967.

Recipients of the four awards to begin July 1, 1983 are:



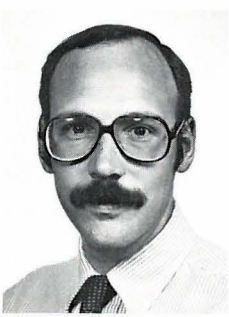
Frank L. Douglas, M.D., Ph.D.

- Frank L. Douglas, M.D., Ph.D., Assistant Professor, Department of Medicine, Committee on Clinical Pharmacology, University of Chicago. Dr. Douglas' research will involve an investigation of the role of neuropeptides and interaction of neuropeptides and catecholamines in the control of blood pressure. Experimental animals will include both neonates and adults of two strains of normotensive rats and spontaneously hypertensive rats. Electrolytic and chemical lesions will be made in specific brainstem nuclei in neonates and adults, and correlations will be made between the development or retardation of hypertension and alteration in levels of substance P, somatostatin, vasopressin, and the biogenic amines. Investigation of the response of treated animals to the infusion of norepinephrine and other pressor agents will be carried out. *In vitro* preparations of isolated canine arteries will also be used to attempt to elucidate the mechanism of the vasoaction of the neuropeptides, substance P, and neurotensin. Human clinical investigations will center on the mechanism of the antihypertensive action of oral dopamine analogs and centrally acting adrenergic blockers.



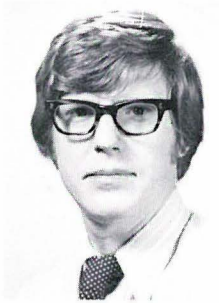
Garret A. FitzGerald, M.Sc., M.D.

- Garret A. FitzGerald, M.Sc., M.D., Assistant Professor, Departments of Medicine and Pharmacology, Vanderbilt University, School of Medicine. Dr. FitzGerald's research interests are in characterizing the physiological importance of arachidonic acid metabolites and their relevance to platelet vascular interactions in man. A major objective of his work has been to relate kinetic parameters of platelet inhibitory drugs to their effect upon *in vivo* and *ex vivo* indices of platelet function and upon endogenous thromboxane and prostacyclin biosynthesis in human models of platelet activation. Additionally Dr. FitzGerald is studying the role of arachidonic acid metabolites in aspirin sensitive and allergic asthma and in pregnancy induced hypertension.



David W. Nierenberg, M.D.

- David W. Nierenberg, M.D., Assistant Professor, Departments of Medicine and Pharmacology & Toxicology, Dartmouth Medical School. Dr. Nierenberg's research efforts begin from the point that some but not all weak organic acid drugs are capable of inhibiting the tubular secretion of methotrexate (MTX) to a clinically important extent, thus enhancing the direct toxicity of MTX. Fatal or near-fatal drug interactions with MTX have been reported with phenylbutazone, penicillin, and furosemide, all weak organic acids. There are many other weak organic acid drugs, and any could be a potential inhibitor of MTX tubular secretion. To investigate which of these drugs are most likely to inhibit the active tubular secretion of MTX, an *in vitro* model of these processes utilizing MTX uptake by rabbit kidney slices will be employed. The ability of a variety of weak organic acid drugs to competitively inhibit the active accumulation of tritiated MTX by rabbit kidney slices will be investigated. The predictions of this model will be further tested by both MTX and a weak organic acid drug for underlying conditions (e.g. psoriasis, arthritis, or cancer).



John W. Turk, M.D., Ph.D.

• John W. Turk, M.D., Ph.D., Assistant Professor, Departments of Medicine, Pharmacology, Washington University School of Medicine. Dr. Turk's research is stimulated by the circumstantial evidence that E-series prostaglandins may inhibit and that arachidonate lipoxygenase products may enhance insulin secretion. Little information exists about how arachidonic acid is metabolized by pancreatic islet cells and whether the activities of these pathways are influenced by stimuli for peptide hormone secretion. His investigations will include the isolation and identification of all major arachidonate metabolites from isolated pancreatic islets, using high performance liquid chromatographic isolation of the compounds and their characterization by ultraviolet spectroscopy and gas chromatography-mass spectrometry; the evaluation of the role of the identified arachidonate metabolites in modulating peptide hormone secretion; and the determination of whether the arachidonic acid hydroperoxides can exert toxic efforts on beta cells. Dr. Turk believes that the results of the study may broaden the understanding of the biochemical events involved in the regulation of peptide hormone secretion and suggest means for the pharmacologic manipulation of these processes.

Those individuals whose awards began July 1, 1982 are:

• Brian B. Hoffman, M.D., Assistant Professor, Departments of Medicine and Pharmacology, Stanford University School of Medicine.

• Janice B. Schwartz, M.D., Instructor, Section of Cardiology and Section of Hypertension and Clinical Pharmacology, Baylor College of Medicine.

• Jack P. Uetrecht, M.D., Ph.D., Assistant Professor, Departments of Pharmacology and Medicine, Vanderbilt University School of Medicine.

Those individuals who entered their second year of awards in July, 1982 are:

• Brian Leyland-Jones, M.B., M.S., Assistant Professor, Department of Pharmacology and Medicine, Cornell University Medical College.

• John R. Luderer, M.D., Assistant Professor, Departments of Medicine and Pharmacology, Pennsylvania State University College of Medicine.

• James A. Nathanson, M.D., Ph.D., Associate Professor, Department of Neurology, Harvard Medical School.

• Juerg Reichen, M.D., Assistant Professor, Department of Medicine, University of Colorado School of Medicine.

• Branimir I. Sikic, M.D., Assistant Professor of Medicine, Division of Oncology, Stanford University School of Medicine.

Those individuals whose awards continued for a third year beginning July 1, 1982 are:

- Ka Kit Hui, M.D., Assistant Professor, Department of Medicine, University of California, Los Angeles, School of Medicine.

- Richard D. Mamelok, M.D., Assistant Professor of Medicine and Pharmacology, Department of Medicine, Stanford University School of Medicine.

- Alastair J. J. Wood, M.B., Ch.B., M.R.C.P., Associate Professor, Departments of Medicine and Pharmacology, Vanderbilt University School of Medicine.

Those individuals who concluded their awards in 1982 are:

- Christopher S. Wilcox, M.D., Ph.D., Assistant Professor, Department of Medicine, Harvard Medical School.

- Thorir D. Bjornsson, M.D., Assistant Professor of Pharmacology and Medicine, Division of Clinical Pharmacology, Duke University Medical Center.

Geographical distribution of Foundation awards under the "Faculty Development Awards in Clinical Pharmacology" program, 1967-1983.

● One
○ More than One

Fellowships for Careers in Clinical Pharmacology

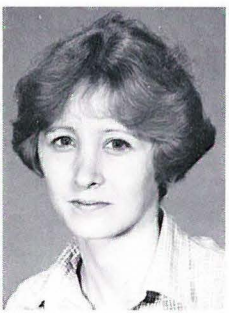
The second program provides Fellowships for Careers in Clinical Pharmacology. This award offers clinicians an opportunity for intensive study in any of the basic sciences that fall within the general field of pharmacology. The program is open to physicians, dentists and veterinarians who are well into their clinical training and wish to pursue careers in clinical pharmacology. With the year or two of support offered by this fellowship program, depending on the particulars of the undertaking, the individual can pursue full-time the basic pharmacologic sciences needed to complement his clinical skills.

The program was amended in 1982 to allow an individual to apply for a fellowship two years in advance of the activation date of the award. For example, those applying for a fellowship in

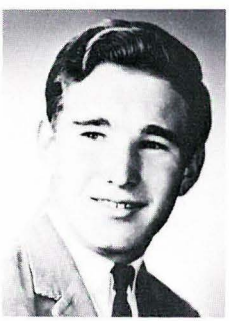
the fall of 1983 may elect to ask that the fellowship be for July 1984 or July 1985.

The first awards under this program were made in 1973. Since that time, thirty fellowships have been awarded.

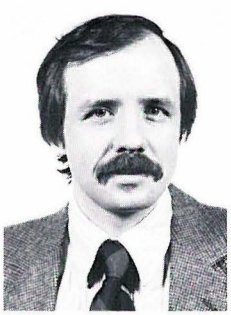
Recipients of the four fellowships beginning July 1, 1983 are:


Bonnie S. Glisson, M.D.

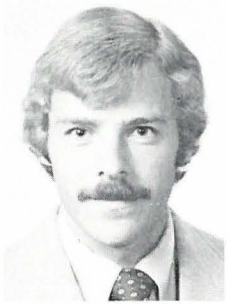
- Bonnie S. Glisson, M.D., Fellow, Division of Medical Oncology, Department of Medicine, University of Florida College of Medicine. Dr. Glisson's research efforts will focus on the mechanism of action of a new anticancer agent VP-16. This agent has become an extremely useful agent in the treatment of germ cell tumors, lymphomas and small cell lung cancer. She will examine the mechanism by which VP-16 creates breaks in nuclear DNA and how these breaks result in an antitumor effect. Since many tumors are resistant to this drug as with all anticancer drugs it is important that the mechanisms for this resistance also be studied. Such investigations may not only increase understanding of how the drug works but suggest ways of circumventing the resistance thus increasing the antitumor effect.


Andrew Guterman, M.D., Ph.D.

- Andrew Guterman, M.D., Ph.D., Fellow, Department of Neurology, University of Miami School of Medicine. Dr. Guterman's research training will deal with the pharmacokinetics of anticonvulsants. He will be involved in Phase II and III studies of a potential anticonvulsant. During an elective period during earlier training he had participated in the Phase I work on the compound. In a second phase of his research commitment, he will be involved in studies of the interaction of Carbamazepene with other concurrent anticonvulsants in patients as well as studies of the alteration of Phenytoin kinetics in uremic patients using stable isotopes of these two agents and triple quadrupole mass spectroscopy. In a final study, Dr. Guterman will be studying the tissue kinetics for Paraldehyde and Lorazpam in the CNS in cats, allowing a determination of bioavailability and half-life.


Ralph A. Kelly, M.D.

- Ralph A. Kelly, M.D., Fellow, Department of Clinical Pharmacology, Harvard Medical School. Dr. Kelly plans to examine the evidence from research in humans and in animals regarding salt intake and blood pressure which points to a hormone circulating in the blood which could both enhance salt excretion by the kidney and elevate blood pressure. He intends to investigate the role of this hormone which is chemically related to the drug, digoxin. He will measure this endogenous digoxin-like material or "endoxin" in the blood of rats to test whether it is released in response to changes in the amount of salt in the diet. Hypertensive rats will be given an antibody which blocks the action of digoxin and measurement of any changes in salt excretion or blood pressure will be made. From this, he hopes to be able to assess the role of endoxin in the regulation of the function of the kidneys and the blood vessels in hypertension.



Jonathan R. Wispe, M.D.

- Jonathan R. Wispe, M.D., Fellow, Departments of Pediatrics and Pharmacology, University of Iowa College of Medicine. Dr. Wispe's research project involves the measurement of expired gases (ethane, pentane, etc.) in neonates with a variety of clinical problems. The use of this technique has enjoyed considerable laboratory experience in experimental animals and is believed to represent a critical evaluation of the quantitative aspects of lipid peroxidation. With this methodology, Dr. Wispe hopes to develop a rigorous evaluation and examination of the role of lipid peroxidation in selected clinical problems of the neonate (RDS, BPD) and specifically to access the utility of vitamin E therapy in amelioration or modification of these lipid peroxidation reactions. The results of the volatile gas experiments will be compared with more traditional parameters of lipid peroxidation, including TBA reactants and serum peroxy acid measurements. The results of these experiments should provide insight into the utility and rationale for the proposed use of vitamin E for treatment and prevention of retrolental fibroplasia and chronic lung disease in infants.

Those individuals whose fellowships began July 1, 1982 are:

- Eric P. Brass, M.D., Fellow, Division of Clinical Pharmacology, University of Washington School of Medicine.

- Thomas A. Kent, M.D., Fellow, Department of Psychiatry, University of Kansas College of Health Sciences and Hospital.

- Howard R. Lee, M.D., Fellow, Department of Pharmacology, University of Arizona College of Medicine.

- Mark S. Smith, M.D., Fellow, Clinical Pharmacology Division, Duke University School of Medicine.

The individual whose fellowship entered the second year of the award on July 1, 1982 is:

- Richard P. Day, M.D., Fellow, Department of Medicine, University of Washington School of Medicine.

Those individuals whose awards concluded in 1982 are:

- Cheryl Mahony, M.D., Fellow in Cardiology, Department of Medicine, Duke University Medical Center.

- Theodore Wang, M.D., Research Fellow, Division of Clinical Pharmacology, Vanderbilt University School of Medicine.

- Jeffrey R. Wilcke, D.V.M., Fellow, Department of Veterinary Medicine and Veterinary Biosciences (Pharmacology), University of Illinois College of Veterinary Medicine.

- Linda A. Linday, M.D., Departments of Pharmacology and Pediatrics, Cornell University Medical College, resigned her fellowship to take employment with Knoll Pharmaceutical Company.

Geographical distribution of Foundation awards under the "Fellowships for Careers in Clinical Pharmacology" program, 1973-1983.

● One
○ More than One

Medical Student Research Fellowships in Pharmacology-Clinical Pharmacology

The third program is the Medical Student Research Fellowships in Pharmacology-Clinical Pharmacology. This program, which began in 1974, provides students an opportunity to spend up to one year full-time conducting an investigative project in pharmacology-clinical pharmacology. The minimum period of the award is three months. It is hoped that by having students become involved in investigative projects at a point when career choices are still relatively flexible, that they will opt for research careers in clinical pharmacology. Forty-nine awards have been made since 1974.

The five students whose fellowships began July 1, 1982 are:

● Daniel Becker, Stanford University School of Medicine, has a three month fellowship which is being conducted at Harvard Medical School. His principal advisor is Dr. Stanley Goldin, Assistant Professor, Department of Pharmacology, Harvard Medical School. Mr. Becker's research is a continuation of earlier work during his undergraduate years. A number of inorganic and organic cations can compete with sodium for an anionic site on the sodium channel protein. It also has been demonstrated that such competition exists as well between the cationic toxins of saxitoxin (STX) and tetrodotoxin and a variety of inorganic cations in nonmyelinated preparations. Studies of binding of STX to central nervous system axolemma have confirmed in this system that the apparent STX equilibrium dissociation constant (K_D) was strongly affected by the cationic environment. Cs^+ increased the K_D in a simple competitive manner. In contrast, Na^+ was shown to exert a highly cooperative inhibition at concentrations between 75 and 200 mH. This suggested that the interaction between Na^+ and the saxitoxin binding site might serve a physiological function. The STX binding site of mammalian myelinated axons might mediate a sodium-sensitive modulation of sodium channel function by an unidentified endogenous substance.

Mr. Becker's initial work involved a search for this postulated endogenous factor in the mammalian central nervous system. A

series of experiments found evidence of such a factor. The current research examined the possibility of a physiological function for the factor. The further work during the fellowship showed that the material whose effects were earlier observed is choline, the inhibition of action potentials occurring at concentrations which preclude any physiological role for it as a modulator of voltage-sensitive sodium channels.

- Thomas C. Chelimsky, Washington University School of Medicine, has a three month fellowship. His principal advisor is Dr. Clifford Saper, Assistant Professor, Department of Neurology. The selective decreases in cortical levels of acetylcholine (Ach) in patients with senile dementia of the Alzheimer type (SDAT) is known, but its precise functional and therapeutic implications remain unclear. Evidence tends to support a cholinergic role in memory and cognitive function. It has been hypothesized that the decreased Ach levels in the cortex of SDAT patients may be related to the short-term memory disorder characteristic of the disease.

  Mr. Chelimsky is studying the magnocellular basal nucleus in the substantia innominata. Evidence suggests that this system is cholinergic in nature. He is examining in detail the cholinergic afferents to the cortex, using a double label technique. By a systematic mapping of cholinergic cortical projections he hopes to demonstrate new insights into the connections of the Ach system.

- Randall J. Lee, University of California, Los Angeles, School of Medicine, has a year-long fellowship. His principal advisor is Dr. Peter Lomax, Professor of Pharmacology. Mr. Lee is involved in a study of epilepsy. Using the mongolian gerbil, he is investigating brain receptor differences between seizure prone animals and seizure resistant animals. He is concerned with Gaba, benzodiazepene, Ach and dopamine receptors. The study will compare differences in receptor affinity and number between the two groups at various stages of seizure activity.

  In addition to that research, Mr. Lee is also involved with a project concerned with the beta blocker rebound phenomenon. It has been reported that rats chronically treated with propanolol show an increase in cardiac beta-adrenergic receptors. This suggests that a receptor change may be responsible for this phenomenon. The specific project that he is involved in is a pre-clinical study on rats comparing two beta blockers, propanolol and pindolol.

- Jeffrey A. Ross, Ohio State University School of Medicine, has a year-long fellowship. His principal advisor is Dr. Joseph R. Bianchine, Professor and Chairman, Department of Pharmacology. Mr. Ross is studying the pharmacokinetics and disposition studies of Phenytoin in the rat treated with a perfluorochemical blood substitute. Initial findings from other studies appear to support the hypothesis that the use of artificial blood substitutes may alter the disposition of drugs and foreign chemicals in

humans. Because of this, modification of drug therapy may be in order to avoid undesirable side effects as use of these artificial blood substitutes increases.

● James A. Scott, University of Florida, has a year-long fellowship. His principal advisor is Dr. Fulton T. Crews, Assistant Professor of Pharmacology. Mr. Scott is studying in rats the interactions between the adrenergic and serotonergic systems and how interactions relate to the etiology of depression and the action of antidepressants and other drugs, e.g., trytophan, lithium, electroconvulsive shock, in combination with α-antagonists. The effects of these treatments on cerebral cortical β-receptor and $5HT_2$ receptor density will be determined.

It is possible that the inhibitory α_2 receptor represents the link between the action of antidepressants on these two monoamine systems in the brain. Therefore, a second series of experiments will determine the effects of chemically lesioning the central noradrenergic and serotonergic nerves on the central receptors and their responses to antidepressants. The changes in receptor density after selective lesions of the adrenergic or serotonergic nerves will clarify the interaction of these two monoamine systems with each other as well as with antidepressants.

Geographical distribution of Foundation awards under the "Medical Student Research Fellowships in Pharmacology-Clinical Pharmacology" program, 1974-1982.

● One
○ More than One

Clinical Pharmacology Unit Support

This program is designed to assist directors of clinical pharmacology units established within the prior two years of the award and for units with a change in directorship during that period. The grant provides a total of $50,000 which may be used at any time during a three-year period. The program is aimed at providing some initial funds to enable the unit's research efforts to be maintained until other research grants are obtained. The first grants were made in 1978. The total number of awards made to date is eight.

The awards beginning July 1, 1982 were made to:

- Division of Clinical Pharmacology, Department of Pharmacology and Department of Pediatrics, University of South Alabama College of Medicine. The Division was formed in November, 1981. Robert C. Boerth, M.D., Ph.D., Professor of Pharmacology and Pediatrics is the director. The division has several research projects underway in the area of myocardial toxicity of Adriamycin. Plans are underway to study the effects of aging on the pharmacokinetics and pharmacodynamics of cardiac drugs. Other research initiatives involve antihypertensive drugs influences on hemodynamic response to exercise in children and adolescents; perinatal development of responses in pulmonary vascular smooth muscle (aimed at characterizing the responses of the neonatal pulmonary vasculature to hypoxic stimuli and to determine which drugs or drug combinations can selectively produce pulmonary vasodilation and reduce the pulmonary vascular response to hypoxia); and the renal pathology of oxygen free radicals.

- Clinical Pharmacology and Toxicology Unit, Departments of Medicine and Pharmacology, The University of Utah College of Medicine. Douglas E. Rollins, M.D., Ph.D., Assistant Professor of Medicine and Pharmacology was named director of the unit July, 1980. The major basic research efforts of the unit are in the area of hepatic uptake and biliary excretion of drugs; and the production and characterization of monoclonal anti-drug antibodies. The clinical research projects involve primarily the study of the pharmacokinetics of drug disposition.

Geographical distribution of Foundation awards under the "Developmental Grant for Clinical Pharmacology Units" program, 1978-1982.

● One
○ More than One

BASIC PHARMACOLOGY
Faculty Development Awards in Basic Pharmacology

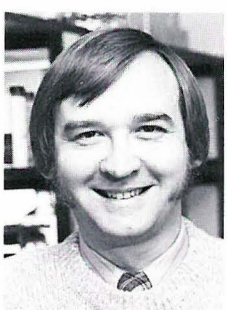
The purpose of these Faculty Development Awards is to strengthen basic pharmacology by helping maintain existing academic capability and, ultimately, to expand it by enlarging the faculty base. To accomplish these goals, support is provided to full-time junior faculty members committed to careers in pharmacology who give promise of outstanding accomplishments.

The first awards, which are for a two-year period, were made in 1973. The program provides salary and fringe benefits. The Foundation has set a ceiling of $25,000 on the amount of its participation in the total yearly salary and fringe benefits for any candidate beginning with the 1980 awards. The total number of awards made to date is thirty-one.

Those who received the awards beginning July 1, 1983 are:

Keith T. Demarest, Ph.D.

- Keith T. Demarest, Ph.D., Assistant Professor, Department of Pharmacology and Toxicology, Michigan State University. Dr. Demarest's research will attempt to characterize changes in the properties of central dopaminergic neurons in acute and chronic estrogen-treated rats and to relate these changes to alterations in behavioral, neurochemical and endocrinological parameters mediated by these neurons. Microchemical techniques will be employed to measure steady-state concentrations and the rate of synthesis and turnover of dopamine in the specific brain regions containing terminals of the nigrostriatal, mesolimbic and tuberoinfundibular-hypophyseal dopamine neuronal systems. Efforts will be made to correlate these changes with estrogen-induced alterations in dopamine receptor binding, anterior pituitary dopamine content and serum prolactin concentrations. The integrity of dopaminergic regulatory mechanisms (autoreceptors, neuronal feedback loops, and prolactin-hormonal feedback) and the responses of these systems to chronic dopamine receptor blockade and partial denervation will also be determined. Efforts will be made to determine which of the observed changes is a direct action of estrogen or a consequence of the estrogen-induced increase in anterior pituitary secretion of prolactin.



Edward Hawrot, Ph.D.

- Edward Hawrot, Ph.D., Assistant Professor, Department of Pharmacology, Yale University School of Medicine. Dr. Hawrot's research is concerned with the use of monoclonal antibodies in the study of mammalian acetylchoine receptors. Monoclonal antibodies will be prepared and used as probes to examine possible structural similarities between acetylcholine receptors of different pharmacological specificity. He hopes that the appropriate monoclonal antibodies raised against the nicotinic, neuromuscular acetylcholine receptor will be capable of identifying molecular regions held in common between the muscle receptor and other types of acetylcholine receptors. His research program will utilize biochemical and immunohistochemical methods to detect, visualize, and characterize cross-reacting antigens in selected tissue sections, cultured cell lines, and primary cultures of muscle and neurons.

George A. Nickols, Ph.D.

- George A. Nickols, Ph.D., Assistant Professor, Department of Pharmacology, Southern Illinois University School of Medicine. Dr. Nickols will be examining the vasodilator effects of parathyroid hormone. The ability of parathyroid hormone to relax arterial strips will be analyzed and correlated temporally with fluctuations in cyclic nucleotide levels. Identification and

characterization of putative parathyroid hormone receptors in isolated vascular smooth muscle cells via direct radioligand binding studies will be performed. Also, the interaction of parathyroid hormone with adenylate cyclase of vascular smooth muscle cells will be studied. It is hoped that these investigations will provide new information as to the physiologic function of parathyroid hormone in the cardiovascular system.

Those who began their awards July 1, 1982 are:

- Walter R. Dixon, Ph.D., Assistant Professor, University of Kansas School of Pharmacy.
- Jerry M. Farley, Ph.D., Assistant Professor, Department of Pharmacology and Toxicology, University of Mississippi Medical Center.
- Gregory A. Weiland, Ph.D., Assistant Professor, Department of Pharmacology, New York State College of Veterinary Medicine.

Those who entered the second year of their awards on July 1, 1982 are:

- Allyn C. Howlett, Ph.D., Assistant Professor, Department of Pharmacology, St. Louis University School of Medicine.
- Edwin K. Jackson, Ph.D., Assistant Professor, Department of Pharmacology, Vanderbilt University School of Medicine.
- Kenneth P. Minneman, Ph.D., Assistant Professor, Department of Pharmacology, Emory University School of Medicine.

Those whose awards concluded in 1982 are:

- Ted H. Chiu, Ph.D., Associate Professor, Department of Pharmacology, Medical College of Ohio.
- Paul H. Fischer, Ph.D., Assistant Professor, Department of Human Oncology, University of Wisconsin.
- Lindsay B. Hough, Ph.D., Assistant Professor, Department of Pharmacology, Mount Sinai School of Medicine.
- Guy Le Breton, Ph.D., Associate Professor, Department of Pharmacology, University of Illinois College of Medicine.

Geographical distribution of Foundation awards under the "Faculty Development Awards in Pharmacology" program, 1978-1983.

● One
○ More than One

Fellowships for Advanced Predoctoral Training in Pharmacology or Toxicology

The program, offered initially in 1977, is designed to assist those candidates who have one or two years remaining in their predoctoral training, the time during which they are engaged in their thesis research.

The fellowship program provides a stipend of $5,040 a year, payment of tuition and $500 a year for incidentals directly associated with the thesis research preparation. The program has been funded to provide eight fellowships each year. However, three extra fellowships were authorized for 1983. A total of sixty-three fellowships have been made since 1977.

Those who received fellowships which begin between January-August, 1983 are:

- Stewart N. Abramson, Department of Pharmacology, University of Colorado Health Sciences Center. Mr. Abramson will be conducting this research with Dr. Perry Molinoff at the University of Pennsylvania. His research is a study of agonist interactions with beta-adrenergic receptors in cultured cell lines.

- Jane F. Amara, Department of Pharmacology, Yale University School of Medicine. Her advisor is Dr. Priscilla S. Dannies, Associate Professor of Pharmacology. Her research will examine whether estrogen's stimulation of pituitary tumor cell growth and stimulation or prolactin are independently mediated.

- Susan L. Brown, Pharmacology Division, Department of Medicine, University of California, San Diego. Her advisor is Dr. Joan Heller Brown, Assistant Professor of Medicine. Ms. Brown's research is concerned with the muscarinic regulation of phosphatidylinositol metabolism in dissociated heart cells.

- David M. Cocchetto, Department of Pharmacology, Duke University School of Medicine. His advisor is Dr. Thorir Bjornsson, Assistant Professor of Pharmacology. His research is aimed at studying the hemostatic system at all levels of thrombus formation and thrombus degradation by use of prototypical pharmacological agents acting at several key steps in the hemostatic cascade.

- David I. Israel, Department of Pharmacology, Stanford University School of Medicine. His advisor is Dr. James P. Whitlock, Jr., Associate Professor. He is studying the induction of cytochrome P-450 in variant mouse hepatoma cells.

- Daniel C. Liebler, Department of Pharmacology, Vanderbilt University School of Medicine. His advisor is Dr. F. Peter Guengerich, Associate Professor of Biochemistry. His research is concerned with the formation and disposition of reactive metabolites in the biotransformation of vinyledine chloride.

- Leslie J. Lipka, Department of Pharmacology, The Medical College of Pennsylvania. Her advisor is Dr. Claire M. Lathers,

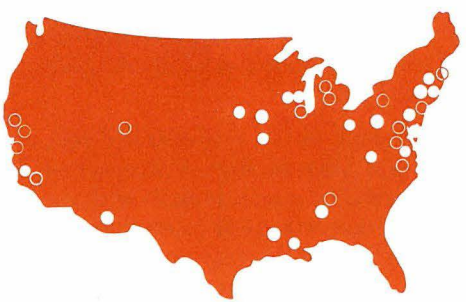
Assistant Professor of Pharmacology. Her research is examining the hypothesis that arrhythmias and death induced by psychotropic agents may be due to their ability to modify autonomic neural control of the heart.

- Mark S. Rappaport, Department of Pharmacology, Northwestern University School of Medicine. His advisor is Dr. Paula Stern, Professor of Pharmacology. His study is examining phospholipids as mediators of parathyroid hormone and vitamin D actions on bone tissue.

- Denise E. Robinson, Department of Pharmacology, Georgetown University School of Medicine. Her advisor is Dr. Richard McGee, Jr., Associate Professor of Pharmacology. Her research is aimed at a study of regulation of neuronal nicotine acetylcholine receptors.

- Karl B. Thor, Department of Pharmacology, Pennsylvania State University. His advisor is Dr. W. C. de Groat, Professor of Pharmacology. His research is aimed at understanding the mechanism of changes in neural control in paraplegics and to generate a pharmacological approach to the treatment of neurogenic bladder dysfunction.

- Daniel R. Van Wagoner, Department of Pharmacology, Thomas Jefferson University School of Medicine. His advisor is Dr. N. Lakshminarayanaiah, Research Professor of Pharmacology. His research is aimed at characterizing the effects of the calcium entry blocking drugs on the calcium channel.



Geographical distribution of Foundation awards under the "Fellowships for Advanced Predoctoral Training in Pharmacology/Toxicology" program, 1972-1983.

● One
○ More than One

Fellowship Awards in Pharmacology-Morphology

The aim of this program is to advance understanding of drug action through the discovery of specifically related cellular and tissue changes; and, concurrently, to uncover associations between normal and abnormal function in particular tissue and cellular structure.

The awards are two years each. The level of support varies and is aimed at keeping within the existing stipends for similarly trained individuals within the applicant university. Since 1968

when the first fellowships were offered, fifty-two awards have been made.

The program requires that the candidate be qualified primarily either in a morphologic specialty or in pharmacology. However, training to be achieved under the fellowship in the complementary discipline need not be formal. The candidate's program should result in a familiarity with a new discipline approach by using his primary discipline as a medium for acquiring the second.

The recipients of fellowships which began July, 1982 are:

Barbara J. Crain, Ph.D., M.D.

- Barbara J. Crain, Ph.D., M.D., Fellow, Departments of Pathology and Pharmacology, Duke University Medical Center. Dr. Crain's research is involved with the role of enkephalins in the hippocampus of kindled rats. Kindling represents an animal model for epilepsy in which repeated administration of an initially subconvulsive electrical stimulus eventually culminates in a generalized seizure. Since hippocampal metenkephalins increase hippocampal pyramidal cell firing rates, the hypothesis she is testing is that kindling alters enkephalin-mediated neuronal communication in the Hippocampus. These experiments will provide important insights into the process of epileptic attacks and the neuronal circuits involved in seizure disorders. As of December 31, 1982, Dr. Crain resigned the fellowship.

Mark G. Currie, Ph.D.

- Mark G. Currie, Ph.D., Postdoctoral Fellow, Department of Pharmacology, Washington University School of Medicine, St. Louis. Dr. Currie's research is aimed at the study of the biosynthesis and function of renal prostaglandins. He intends to determine the specific sites along the nephron that possess the biosynthetic capacity to produce prostaglandins. This uses a variety of biochemical, pharmacological, morphological and tissue culture techniques.

Linda M. Marshall, Ph.D.

- Linda M. Marshall, Ph.D., Postdoctoral Fellow, Departments of Pharmacology and Microbiology, University of Texas, San Antonio. Dr. Marshall's research deals with the biochemical and pharmacological interactions of calmodulin in receptor mediated endocytosis. The aims are to use a number of drugs that inhibit different stages of endocytosis to identify membrane receptors for various drugs and to determine their fate after endocytosis; quantify receptor characteristics during time course regimens of drug exposures; and to raise monoclonal antibodies calmodulen and clathrin as molecular probes to compare specific site interactions with ligand receptor complexes.

Those individuals who entered the second year of their fellowships in 1982 are:

- Stanley R. Jolly, Ph.D., Postdoctoral Fellow, Department of Pharmacology, University of Michigan Medical School.

- Iris Nemhauser, Ph.D., Postdoctoral Fellow, Department of Pharmacology, Columbia University College of Physicians and Surgeons.

- Howard Ratech, M.D., Fellow, Departments of Pathology and Medicine, New York University Medical Center.

Those individuals whose fellowships concluded in 1982 were:

- Paulette Bernd, Ph.D., Fellow, Department of Pharmacology, New York University School of Medicine.

- Shew Y. Chan, Ph.D., Research Fellow, Department of Pharmacology, Harvard Medical School.

- Jay R. Knutson, Ph.D., Research Associate, Department of Biology, The Johns Hopkins University, School of Arts and Sciences.

Geographical distribution of Foundation awards under the "Fellowship Awards in Pharmacology-Morphology" program, 1968-1982.

● One
○ More than One

Faculty Awards in Toxicologic Pathology

Gerald G. Long, D.V.M., Ph.D.

There is a need to attract academic scientists interested in analyzing, reviewing and questioning where appropriate the present state of the art in the field of toxicology. To examine the degree of interest the academic community may have, a junior faculty program was authorized for a three year period. The goal of the program is to attract veterinary and comparative pathologists who are interested in spending two years in drug toxicology research. During the pilot period, a total of three awards is anticipated. For 1983, two of the three awards were made.

Those individuals whose awards begin July 1, 1983 are:

- Gerald G. Long, D.V.M., Ph.D., Assistant Professor, Department of Veterinary Microbiology, Pathology and Public Health, Purdue University School of Veterinary Medicine. Dr. Long's research will be directed toward establishing a research area to characterize mechanisms of embryotoxicity. Emphasis will be placed on mechanisms of injury that occur during the early embyonic period. Mycotoxins will be used as specific agents of injury.

Glen K. Miller, D.V.M., Ph.D.

- Glen K. Miller, D.V.M., Ph.D., Assistant Professor, Department of Pathology, Colorado State University College of Veterinary Medicine and Biomedical Sciences. Dr. Miller's research is aimed at the study of the immunotoxicology of glucocorticosteroids as a model to further understanding of how prenatal exposure to

drugs and chemicals may injure the developing immune system. Quantitative morphology of lymphoid and endocrine organs will be correlated with functional studies in the neonatal and young adult beagle dog. It is of particular concern to evaluate the relationship between fetal age at exposure, injury to specific lymphoid organs, and the effects of steroids upon postnatal immunocompetency.

Geographical distribution of Foundation awards under the "Faculty Awards in Toxicologic Pathology" program, 1982-1983.

● One
○ More than One

RESEARCH GRANTS

An important aspect of the PMA Foundation effort has been the support of fundamental research in drug toxicology. Between 1966 and 1971, 26 research grants of relatively large amounts for two to five years were awarded, principally to established investigators to either extend existing research or to provide "seed" monies to follow a promising lead. In 1971, a change in emphasis within the Foundation's programs shifted the bulk of the funds into educational support programs and, therefore, less into research. The Foundation does, however, continue to accept requests for support and suggestions for pertinent research projects since it is important that the potential within the Foundation for helping that particularly promising effort be maintained.

Geographical distribution of Foundation general research grants, 1966-1982.

● One
○ More than One
★ Outside U.S.

Research Starter Grants

As part of the change of emphasis in 1971 which sought to direct monies more toward the development of the individual, a program of Research Starter Grants was initiated. These grants are intended to provide financial support for beginning investigators. The program allows for approximately 20 research starter grants each year. The first awards were made in 1972. A

total of 290 research starter grants have been made, including the twenty-three awards beginning January 1, 1983.

The recipients of the grants beginning January 1, 1983 are:

WILLIAM D. ATCHISON, Ph.D.
Michigan State University
College of Veterinary Medicine

DONALD M. COEN, Ph.D.
Harvard University
School of Medicine

JOSEPH COHEN, Ph.D.
Howard University
Graduate School of Arts & Sciences

KEITH T. DEMAREST, Ph.D.
Michigan State University
College of Osteopathic Medicine

MARGARITA L. DUBOCOVICH, Ph.D.
Northwestern University
School of Medicine

WILLIAM C. ELLIOTT, M.D.
State University of New York, Syracuse
College of Medicine

FRANK J. GORDON, Ph.D.
Emory University
School of Medicine

DAVID W. HEIN, Ph.D.
Morehouse School of Medicine

ROBERT E. HRUSKA, Ph.D.
State University of New York, Buffalo
School of Pharmacy

RICHARD S. JOPE, Ph.D.
University of Alabama in Birmingham
School of Medicine/Dentistry

CHRISTOPHER J. LINGLE, Ph.D.
The Florida State University
College of Arts and Sciences

EDWIN M. MEYER, Jr., Ph.D.
University of Florida
College of Medicine

SUSAN C. MILLER, Ph.D.
University of Minnesota
College of Pharmacy

GEORGE A. NICKOLS, Ph.D.
Southern Illinois University
School of Medicine

TREVOR M. PENNING, Ph.D.
University of Pennsylvania
School of Medicine

STEVEN L. PETERSON, Ph.D.
Texas A & M University
College of Medicine

YASUKO RIKIHISA, Ph.D.
Virginia Polytechnic Institute
College of Veterinary Medicine

ROBERT E. SHERIDAN, Jr., Ph.D.
Georgetown University
School of Medicine/Dentistry

CHARLES A. SNINSKY, M.D.
University of Florida
College of Medicine

CHARLES T. STIER, Jr., Ph.D.
New York Medical College

JEROME TRZECIAKOWSKI, Ph.D.
Texas A & M University
College of Medicine

JOHN W. TURK, M.D., Ph.D.
Washington University
School of Medicine

JOHN A. WASSERSTROM, Ph.D.
University of Chicago
Pritzker School of Medicine

Review of the need of the 23 research starter grantees whose awards began January 1, 1982 for a second year of the awards resulted in 17 of them having their awards continued. These are:

PETER W. ABEL, Ph.D.
Emory University
School of Medicine

CHRISTOPHER C. BENZ, M.D.
Yale University
School of Medicine

JEAN M. BIDLACK, Ph.D.
University of Rochester
Center for Brain Research

JOHN Y. L. CHIANG, Ph.D.
Northeastern Ohio Universities
College of Medicine

THOMAS P. DAVIS, Ph.D.
University of Arizona
College of Medicine

EDWARD D. FRENCH, Ph.D.
University of Maryland
MD Psychiatric Research Center

LARRY P. GONZALEZ, Ph.D.
University of Illinois
College of Medicine

KATHERINE A. KENNEDY, Ph.D.
George Washington University
School of Medicine

THOMAS J. MURRAY, Ph.D.
Washington State University
College of Pharmacy

HUGH C. PALFREY, Ph.D.
University of Chicago
School of Medicine

WALTER C. PROZIALECK, Ph.D.
Philadelphia College of
Osteopathic Medicine

LARRY R. STERANKA, Ph.D.
Indiana University
School of Medicine

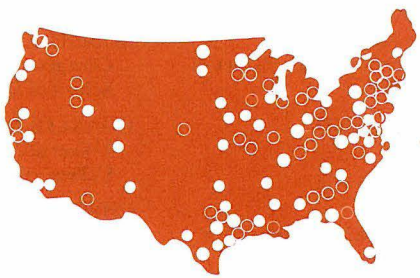
JACK P. UETRECHT, Ph.D., M.D.
Vanderbilt University
School of Medicine

KENDALL B. WALLACE, Ph.D.
University of Minnesota, Duluth
College of Medicine

GREGORY A. WEILAND, Ph.D.
Cornell University
New York State College
of Veterinary Medicine

DOUGLAS M. WILKISON, Ph.D.
Medical College of Wisconsin

GAROLD S. YOST, Ph.D.
Washington State University
College of Pharmacy



Geographical distribution of Foundation awards under the "Research Starter Grants" program, 1972-1983.

● One
○ More than One

OTHER SUPPORT

A grant of $10,000 was made to American Society for Pharmacology and Experimental Therapeutics to aid in the publication of the proceedings of the World Conference on Clinical Pharmacology & Therapeutics scheduled for July 31-August 5, 1983.

A grant of $199,423 was made to the Medical University of South Carolina on behalf of Alan R. Shapiro, M.D., Associate Professor in Family Medicine and Biometry, for testing methods of gathering information on non-hospitalized patients' drug experiences, particularly adverse drug reactions. After some months of effort in attempting to secure the necessary staff and resources to initiate the work of the grant, Dr. Shapiro resigned in early 1983 as principal investigator and the grant was terminated.

PURPOSE

The PMA Foundation was established to promote the betterment of public health through scientific and medical research, with particular reference to the study and development of the science of therapeutics. In achieving this goal, the Foundation plans and initiates scientific and medical research activities, collects and disseminates the results of these activities, and provides financial support and aid to individuals or institutions whose purposes are scientific, educational or charitable.

Certain guidelines have been developed to promote the wise and proper use of the limited resources available. The areas of interest which govern the distribution of funds are support of fundamental research on drugs and programs for training personnel in basic and clinical pharmacology and toxicology.

Throughout the year, programs have been supported and developed which provide the means of achieving the goals of the Foundation. Many worthwhile proposals have been submitted. It has been necessary to limit support to those who hold the highest promise of advancing the purposes of the Foundation.

Those areas not supported within the existing guidelines are:

(1) Research on specific drugs. This exclusion is not meant to preclude support of projects which, of necessity, use a number of drugs to establish a methodology or screening program of potential general applicability. It does exclude those efforts primarily aimed at learning more about specific drugs or classes of drugs.

(2) Funds for construction. The Foundation is not unmindful of the needs and the tremendous pressures for private funds for construction projects. However, it is believed that the scientific community can be better served by channeling the Foundation's available resources into other areas.

(3) Funds for travel.

(4) Funds to cover entertainment costs.

In 1971, the Board of Directors authorized a major shift in program emphasis. While Foundation support of research continues, such support is to be primarily available in a redirected fashion such as the Research Starter Grants program discussed on page 20.

In line with this change of emphasis, the Foundation is expanding support within its current educational programs as outlined in the Education and Training Programs Section on page 4. While meetings have never received a large portion of the support dollar, only in very exceptional circumstances will meetings receive support in the future.

FOUNDATION FINANCES

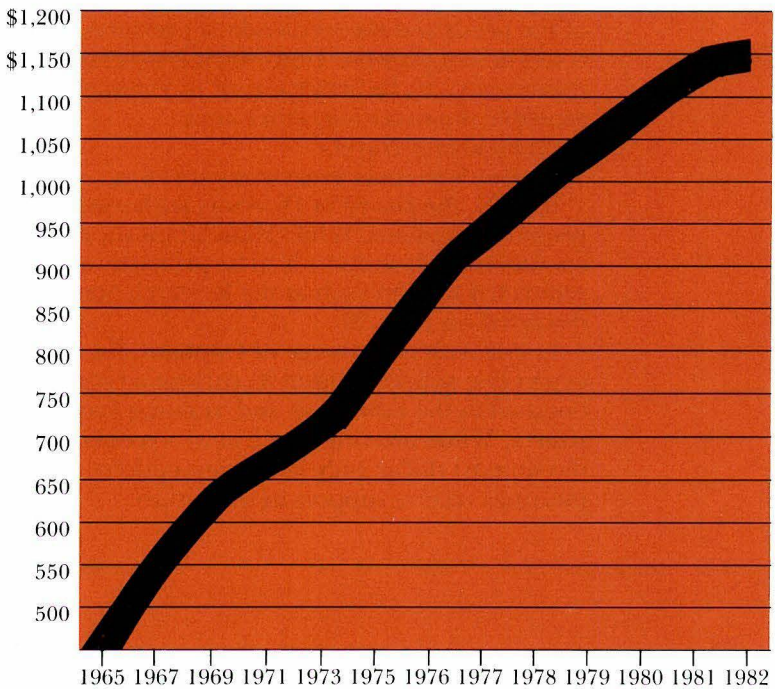
The total income of the Foundation in 1982 was $1,458,811. Of this amount, $1,163,237 came from contributions. The balance of $295,574 came from the restricted fund for the postmarketing monitoring grant, investments and refunds of unexpended balances from grants.

Contributions were received from approximately four out of every five PMA Member Firms. Contributions were also received during 1982 from individuals and other groups in the health field.

Grants, Foundation-sponsored programs and other expenses for 1982 amounted to $1,523,327. Of this total, $1,232,627 represent expenditures for grants. There was a fund balance of $1,671,751 as of December 31, 1982. This figure, however, does not reflect the tentatively authorized, undisbursed funds for some of the grants and programs described earlier. The Foundation reports these amounts as expenditures when the funds are disbursed. As of December 31, 1982, the contingency liability for 1983 was approximately $1,110,695.

The Foundation's financial position as of December 31, 1982 has been audited by the Washington, D.C. accounting frim of Buchanan & Company.

PMA Foundation
Contribution Income
1965-1982 (Thousands)



Statement of Income and Expenditures For the Year Ended December 31, 1982

Income

Contributions—Note A	$1,163,237
Restricted Fund—Postmarketing Grant	69,464
Income from investments	196,560
Gain on Sale of Stock	17,014
Miscellaneous Income	12,536
TOTAL INCOME	$1,458,811

Expenditures

Grants—Note B	
Clinical Pharmacology Faculty Awards	$ 303,549
Clinical Pharmacology Fellowships	85,158
Clinical Pharmacology Unit Support	74,520
Basic Pharmacology Faculty Awards	162,500
Medical Student Research Fellowships	21,000
Pharmacology-Morphology Fellowships	110,440
Research Starter Grants	260,000
Advanced Predoctoral Fellowships	145,996
Postmarketing Monitoring Grant	69,464
	$1,232,627
Administrative, December Awardee Meeting and Special Toxicology Workshop Expenses	$ 290,700
TOTAL EXPENDITURES	$1,523,327
Excess of expenditures over income	$ 64,516
General fund balance at January 1, 1982	$1,736,267
General fund balance at December 31, 1982	$1,671,751

Note A—The Foundation received contributions of $257,833 prior to December 31, 1982 which the Foundation considered applicable to 1983 and, therefore, not recorded as income in 1982.

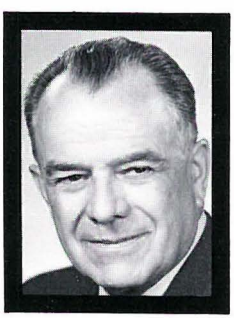
Note B—In addition to the amounts shown, the Foundation has committed itself, subject to annual review, to make certain grants. At December 31, 1982, the amounts still to be disbursed with respect to these grants during 1983 amounted to approximately $1,110,695.

ORGANIZATION AND ADMINISTRATION

The PMA Foundation operates through its officers and four advisory committees. In April, 1982, Irwin Lerner, President and Chief Executive Officer, Hoffmann-La Roche Inc., was elected Chairman of the Board. Albert J. Frey, Ph.D., Chairman, Sandoz, Inc., was elected Vice Chairman, and Verne M. Willaman, Executive Committee Member and Member of the Board of Directors, Johnson & Johnson, was elected Secretary, Treasurer. Thomas E. Hanrahan is President and Irwin C. Winter, M.D., Ph.D., serves as staff consultant.

Irwin Lerner

Thomas E. Hanrahan



Raymond M. Rice, M.D.

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Albert J. Frey, Ph.D., Vice Chairman
Verne M. Willaman, Secretary, Treasurer
Thomas E. Hanrahan, President

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Research Triangle Park, North Carolina

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New Brunswick, New Jersey

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Vice President, Biochemicals
E. I. du Pont de Nemours & Company
Wilmington, Delaware

[1]Term Expired April, 1982
[2]Named to the Board of Directors April, 1982

In Memoriam

Dr. Raymond M. Rice, former Vice President of the PMA Foundation, died November 22, 1982. Dr. Rice served with distinction with the Foundation from 1967 to 1971, following his retirement from Eli Lilly and Company as Group Vice President of Science and Medicine. His substantial experience and innovative thinking provided the ingredients so necessary for the Foundation in its early efforts. It is with deep regret that we note his death.

ADVISORY COMMITTEES

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Vice President, Research and Development
Ortho Pharmaceutical Corporation
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Newark, New Jersey

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Professor and Chairman
Department of Medicine
Brown University
Providence, Rhode Island

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Vice President, Regulatory Affairs
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Richmond, Virginia

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Senior Vice President, Medical Director
Pharmaceuticals Division
CIBA-GEIGY Corporation
Summit, New Jersey

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Chairman, Committee on Clinical Pharmacology
Department of Pharmacology and Physiological Sciences
University of Chicago
Chicago, Illinois

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Clinical Research Domestic
Merck, Sharp & Dohme
Research Laboratories
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Ayerst Laboratories
New York, New York

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Vice President, Drug Safety Assessment
Merrell Dow Pharmaceuticals, Inc.
Cincinnati, Ohio

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Department of Pharmacology
Cornell University Medical College
New York, New York

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Professor and Chairman
Department of Pharmacology
University of Oregon
Medical School
Portland, Oregon

E. LEONG WAY, Ph.D.
Professor
Department of Pharmacology
University of California
School of Medicine
San Francisco, California

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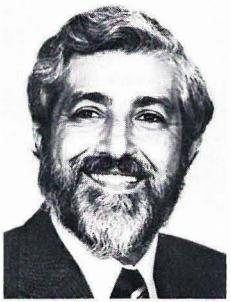
[3]Became Chairman, December, 1982
[4]Resigned April, 1982
[5]New Member April, 1982

Clinical Pharmacology Advisory Committee



Leon I. Goldberg, M.D., Ph.D.

LEON I. GOLDBERG, M.D., Ph.D.
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Chairman, Committee on Clinical Pharmacology
Department of Pharmacological and Physiological Sciences
University of Chicago
Chicago, Illinois

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Clinical Research
Merck Sharp & Dohme Research Laboratories
West Point, Pennsylvania

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Professor and Chairman
Department of Medicine
Brown University
Providence, Rhode Island

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Professor and Chairman
Department of Pharmacology and Therapeutics
State University of New York
Buffalo, New York

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Vice President
Corporate Medical Affairs
Eli Lilly and Company
Indianapolis, Indiana

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Medical Investigator
Veterans Administration Hospital
Palo Alto, California

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Department of Pharmacology
University of Minnesota
Medical School
Minneapolis, Minnesota

ALBERT SJOERDSMA, M.D., Ph.D.
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Merrell Dow Pharmaceuticals Inc.
Cincinnati, Ohio

Toxicologic Pathology Advisory Subcommittee

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Department of Veterinary Microbiology, Pathology and Public Health
Purdue University
School of Veterinary Medicine
West Lafayette, Indiana

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Associate Director of Research and Development
Bristol Laboratories
Syracuse, New York

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Professor
Department of Nutrition and Food Science
Massachusetts Institute of Technology
Cambridge, Massachusetts

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Professor and Chairman
Department of Pharmacology
University of Oregon
Medical School
Portland, Oregon

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Professor and Chairman
Department of Anatomy
Mount Sinai School of Medicine
New York, New York

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Professor and Chairman
Department of Pharmacology
University of Medicine and Dentistry of New Jersey
Newark, New Jersey

FELIX A. DE LA IGLESIA, M.D.
Director, Department of Toxicology
Pharmaceutical Research Division
Warner-Lambert Company
Ann Arbor, Michigan

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