

1976 ANNUAL REPORT
PHARMACEUTICAL MANUFACTURERS
ASSOCIATION FOUNDATION, INC.



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THE BOTTOM LINE

“**H**OW DOES THE BOTTOM LINE READ?” A frequent question these days when assessing the “costs” versus the “benefits” of an activity. The PMA Foundation has yet to have its programs function sufficiently long to reach “the bottom line” but the “subtotals” point to benefits far beyond the amounts authorized for grants over the past eleven years. As a truly long-term investment in the development of the disciplines and knowledge on which the continued vitality of the pharmaceutical industry depends, the support provided through the PMA Foundation ranks extremely high.

The scores of individuals assisted by the Foundation are maturing in their chosen careers and attaining positions of leadership within the academic scientific community. Many of those who received starter grants to get established as independent investigators have gone on to obtain significant additional funding of research related to that begun with the assistance of the Foundation.

A number of the Foundation's faculty awardees have received further recognition from other funding groups: four have received the Burroughs Wellcome Fund Award in Clinical Pharmacology; and four have won Research Career Development Awards from the federal government. Awardee publications have been very numerous.

Academic promotion, of course, significantly measures career growth. Many of those at a junior faculty level at the time of the Foundation award are now associate professors and some, full professors. Directors of eleven clinical pharmacology units are former recipients of Foundation support.

Others who have received fellowships under the unique program which promotes the study of drug action through morphological techniques are at work in the forefront of pharmaceutical research.

These early academic accomplishments of those supported by the Foundation are impressive. Tomorrow's teachers and researchers capable of advancing knowledge in the critical fields of pharmacology and toxicology will undoubtedly come from those aided in their careers through the Foundation's programs.

The Board of Directors, the advisory committees and the generous contributors — as shown by their continuing increase in support of the PMA Foundation — are more than confident that these early successes will expand. The “bottom line” will bring benefits far in excess of costs!

FEEDBACK!

THE SEVENTH IN A SERIES OF YEARLY meetings with recipients of awards under various postdoctoral educational programs and members of the Foundation's advisory committees was held December 6-7, 1976.

W. Clarke Wescoe, M.D., Vice Chairman of the PMA Foundation Board of Directors, opened the meeting with a recap of the Foundation's activities. The keynote speaker for the general session was Avram Goldstein, M.D., Director, Addiction Research Foundation, Palo Alto, California, who covered the topic "Opiate Receptors and Endogenous Opioids". In separate sessions, the clinical pharmacologists, the fellows in pharmacology-morphology and the faculty awardees in basic pharmacology developed their own programs. The clinical pharmacology session was moderated by Leon I. Goldberg, M.D., Ph.D., Chairman of the Clinical Pharmacology Advisory Committee and Chairman, Committee on Clinical Pharmacology, University of Chicago. In this session, guest speaker Robert J. Levine, M.D., Professor of Medicine and Lecturer in Pharmacology, Yale University School of Medicine, spoke on the ethical implications of human research.

The pharmacology-morphology fellows split their time between discussions of the research efforts of some current fellows and the presentation by Dr. Gerald D. Fischbach, Associate Professor of Pharmacology, Harvard Medical School, who talked about his development of a cell culture system for the study of synapse formation.

The faculty awardees in basic pharmacology discussed their research projects.



These yearly meetings continue to provide opportunities to assess how well each program is progressing.

A similar, shorter meeting is held each year with the research starter grantees during the fall meeting of the American Society for Pharmacology and Experimental Therapeutics. Speakers this year were Theodore M. Brody, Ph.D., Professor and Chairman, Department of Pharmacology, Michigan State University and Edward Walaszek, Ph.D., Professor and Chairman, Department of Pharmacology, University of Kansas covering the topic "Computer Assisted Teaching of Pharmacology:" A CATS Presentation.

Such meetings contribute much to the vitality of the PMA Foundation. The opportunities to evaluate each program, to innovate when called for, are greatly enhanced through the interaction between advisory committee members and awardees.



ACTIVITIES

SINCE ITS FORMATION IN 1965, NEARLY \$7 million has been authorized by the PMA Foundation for a variety of workshops, conferences, research projects and educational programs. Of this amount \$2.2 million has been used to support research and about \$4.4 million has gone into educational awards. The remaining \$438,000 has provided financial assistance for scientific meetings, along with a small portion for publications.

As in recent years, virtually all of the 1976 grants and awards were made within the six programs sponsored by the Foundation. These include two faculty level programs of salary and fringe benefit support, three fellowship programs — two postdoctoral and one at the medical student level — and a program of research starter grants for beginning investigators wishing to move into areas of independent research.

Through these programs, the Foundation in 1976 assisted individuals, all of whom were helped at a time crucial in their career development. The Foundation has, in its eleven years of existence, helped about 400 individuals through research and educational support programs.

EDUCATION AND TRAINING PROGRAMS

To further its objectives in the field of education, the PMA Foundation sponsors three programs in clinical pharmacology, one in the combined field of pharmacology-morphology and one in basic pharmacology. Each program is intended to achieve a specific goal, either for a particular rung on an individual's career ladder or in a particular discipline.

A new program will be offered in 1977, with the first awards in January, 1978. This is a fellowship program for advanced predoctoral training in pharmacology/toxicology. The program will provide a stipend, tuition and incidental funds associated with the thesis research efforts of the fellow.

Clinical Pharmacology: The three clinical pharmacology programs provide educational 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 level of support varies, in keeping with the salary structure of the applicant university. The Foundation has set a ceiling of \$30,000 on the amount of its participation in the total yearly salary and fringe benefit for any candidate.

With the new awards scheduled to begin July 1, 1977, a total of 40 individuals have been supported under this program since 1967. They apply for a two-year period, with a third year option.

FACULTY DEVELOPMENT AWARDS IN CLINICAL PHARMACOLOGY

Recipients of the three awards to begin July 1, 1977 are:



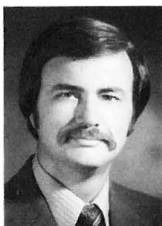
Steven D. Reich,
M.D.

• STEVEN D. REICH, M.D., Associate, Departments of Pharmacology and Medicine, The Medical School, Northwestern University. Dr. Reich's primary responsibility will be to develop a significant research, education and clinical service program in the clinical pharmacology of antineoplastic agents. His research activities will be concerned with the pharmacokinetics and biotransformation of methotrexate and adriamycin in cancer patients and the development of more efficacious drug dosage schedules for combination cancer chemotherapy. Dr. Reich's laboratory provides clinical service of plasma level assays for methotrexate (radioimmunoassay) and adriamycin (spectrophotometric assays) for patients housed in the various hospitals of Northwestern Medical Center. Dr. Reich also participates in the teaching programs in both the Departments of Pharmacology and Medicine as well as in the training of residents, fellows and Ph.D. graduate students.



Reynold Spector,
M.D.

• REYNOLD SPECTOR, M.D., Assistant Professor, Department of Medicine, Harvard Medical School. Dr. Spector is engaged in two areas of clinical pharmacological research, one in the study of medication compliance in an outpatient clinic and a second in the mechanisms of entry of drugs into the central nervous system and the cerebral spinal fluid. Dr. Spector plans to study the usefulness of the nurse practitioner in increasing patient compliance with medication regimens. Compliance with drugs such as digoxin and methyldopa will be monitored by the measurement of their plasma concentrations, and the effect of various interventions by the nurse practitioner will be evaluated. Among the intervention schemes to be monitored will be patient education and medication review. Dr. Spector also proposes to expand his previous studies in the entry of drugs into the spinal fluid by studying the factors which define the pharmacokinetics and the mechanism of transport of vitamin B₆ into the central nervous system. He also plans to extend to therapeutic situations such as brain abscess and brain tumors the results of his animal studies on the entry of antibiotics and chemotherapeutic agents into sites where those agents may be active in the central nervous system. In addition to this research, Dr. Spector will direct the consulting service in clinical pharmacology at the Peter Bent Brigham Hospital.

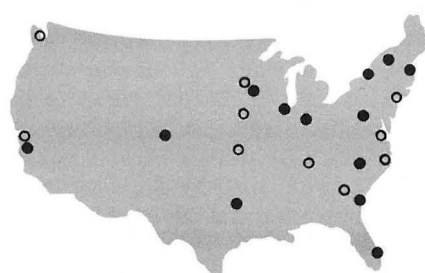


Raymond L.
Woosley, Jr., M.D.,
Ph.D.

• RAYMOND L. WOOSLEY, JR., M.D., Ph.D., Assistant Professor, Departments of Medicine and Pharmacology, School of Medicine, Vanderbilt University. Dr. Woosley intends to pursue two general areas of research. He has worked with members of the

Division of Biomedical Engineering at Vanderbilt to develop techniques for telemetric arrhythmia monitoring and computerized analysis of ventricular arrhythmias. These techniques have been used recently by Dr. Woosley to evaluate the efficacy and pharmacokinetics of tocainide, an investigational antiarrhythmic drug. He now plans to evaluate the antiarrhythmic efficacy of the natural metabolite of procainamide, N-acetylprocainamide, and to compare its side effects and toxicities to the parent compound. Other antiarrhythmic agents to be studied are propranolol and the investigational beta-adrenergic receptor blocking drug, atenolol.

Dr. Woosley's clinical studies with antiarrhythmic drugs led to his interest in studying the mechanism of the procainamide-induced lupus erythematosus syndrome. Dr. Woosley has observed that patients who are phenotypic slow acetylators of procainamide develop antinuclear antibodies and the lupus syndrome earlier than fast acetylators. Dr. Woosley plans to determine the metabolic pathways for procainamide in man and animal models in order to identify potentially toxic metabolites or intermediates and study the mechanism for development of the lupus-syndrome.



Geographical distribution of Foundation awards under its "Faculty Development Awards in Clinical Pharmacology" program, 1967-1977

- One
- More than one

Those individuals whose awards began in July, 1976 are:

- WERNER A. BLEYER, M.D., Assistant Professor, Departments of Pediatrics and Medicine, School of Medicine, University of Washington.
- ROBERT C. BOERTH, M.D., Ph.D., Assistant Professor, Departments of Pediatrics and Pharmacology, School of Medicine, Vanderbilt University.
- CURT R. FREED, M.D., Assistant Professor, Departments of Medicine and Pharmacology, and Acting Head, Division of Clinical Pharmacology, University of Colorado Medical Center.

- JAMES J. LIPSKY, M.D., Instructor, Departments of Medicine and Pharmacology, School of Medicine. The Johns Hopkins University.

Those individuals who entered the second year of their award in July, 1976 are:

- NORBERTO T. DE GUZMAN, M.D., Assistant Professor, Department of Pharmacology, School of Medicine, University of Miami.
- PERRY V. HALUSHKA, Ph.D., M.D., Assistant Professor, Department of Pharmacology, Medical University of South Carolina.

Those individuals whose awards ended in June, 1976 are:

- TERRENCE F. BLASCHKE, M.D., Assistant Professor, Department of Medicine, School of Medicine, Stanford University.
- ROBERT L. CAPIZZI, M.D., Professor and Head, Division of Medical Oncology, Department of Medicine, School of Medicine, University of North Carolina.
- ELSA-GRACE V. GIARDINA, M.D., Assistant Professor, Department of Medicine, College of Physicians and Surgeons, Columbia University.
- RALPH E. KAUFFMAN, M.D., Associate Professor, Departments of Pediatrics and Pharmacology, School of Medicine, University of Kansas.

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

The recipients of the three fellowships beginning July 1, 1977 are:



Thomas P. Green,
M.D.

• THOMAS P. GREEN, M.D., Postdoctoral Fellow, Department of Pharmacology, and Medical Fellow, Department of Pediatrics, University of Minnesota. Dr. Green will investigate the disposition of drugs during human development; to determine how different pathophysiologic states, e.g. renal insufficiency, hepatic insufficiency and altered nutritional states alter sulfo-conjugation. He will also investigate how specific drugs may interfere with sulfo-conjugation during early mammalian development.

Dr. Green will participate in formal course work in pharmacology and take part in the activities of the Division of Clinical Pharmacology such as patient rounds, journal club, and tutorials.



Stanley J. Szefer,
M.D.

• STANLEY J. SZEFLER, M.D., Fellow in Clinical Pharmacology, Department of Pharmacology, School of Medicine, State University of New York. Dr. Szefer's efforts during the tenure of the fellowship will include formal course work in pharmacology and therapeutics; participation in teaching and research activities of the Department of Pharmacology and Therapeutics; and practical experience in clinical investigation in the Department of Pediatrics.

In research, Dr. Szefer will study the renal elimination of drugs, and in particular the renal elimination of catecholamines in laboratory animals. His clinical research will focus on study of the renal elimination of drugs utilizing pharmacokinetic principles, an area in which Dr. Szefer previously worked as a pharmacy student.



Walter M.
Williams, M.D.,
Ph.D.

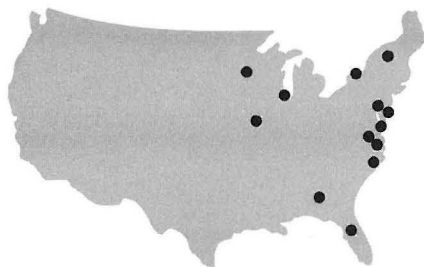
• WALTER M. WILLIAMS, M.D., Ph.D., Fellow in Clinical Pharmacology, Departments of Pharmacology and Medicine, School of Medicine, University of Chicago. Dr. Williams will be involved in projects designed to investigate the effects of antineoplastic agents upon their own metabolism and on the metabolism of two model compounds, antipyrine and indocyanine green. The plasma clearances of the model compounds and selected chemotherapeutic agents will be measured in volunteer patients with carcinoma. Measurements will be made at periodic intervals during the course of chemotherapy. Relationships between the changing pharmacokinetics of antineoplastic drugs and the development of drug resistance or drug toxicity will be investigated. The kinetics of 5-FU disposition will be determined during the first administration of the drug and at periodic intervals thereafter. Prior to each 5-FU kinetic study, antipyrine and indocyanine green clearances will be determined. Dr. Williams will also participate in the clinical pharmacology consulting service and in seminars in medical statistics.

The individual whose fellowship began July, 1976 is:

- WILLIAM P. ARNOLD, III, M.D., Fellow in Medicine and Anesthesiology, Departments of Medicine and Anesthesiology, School of Medicine, University of Virginia.

Those individuals whose awards ended June, 1976 are:

- DAVID M. KORNHAUSER, M.D., Assistant Professor, Departments of Pharmacological and Physiological Sciences, Pritzker School of Medicine, University of Chicago.
- JAMES A. LIPSKY, M.D., Instructor, Departments of Medicine and Pharmacology, School of Medicine, The Johns Hopkins University.
- DOUGLAS N. WEISMANN, M.D., Fellow, Pediatric Clinical Pharmacology Program, College of Medicine, University of Iowa.
- THOM J. ZIMMERMAN, M.D., Associate Professor, Chief, Division of Glaucoma, Louisiana State University.



Geographical distribution of Foundation "Fellowships for Careers in Clinical Pharmacology" program, 1973-1977

• 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 one year full-time in an investigative project in pharmacology-clinical pharmacology. To meet the full-time requirement, the student must interrupt his formal medical training, but he must also intend to continue his schooling at the conclusion of the fellowship. It is hoped that by having students become involved extensively in investigative projects at a point when career choices are still relatively flexible, that they will opt

for research careers in clinical pharmacology. Sixteen awards have been made since 1974.

The PMA Foundation has had a medical student support program since 1968. The earlier program offered three month traineeships to enable students to become acquainted with the techniques used in clinical pharmacology.

The six students who received fellowships which began July 1, 1976 are:

- DANA C. HILT, Tufts University, has completed two years of medical school. His principal advisors are Jane des Forges, M.D., Professor of Medicine, Department of Hematology and Henry G. Mautner, Ph.D., Professor and Chairman, Department of Biochemistry and Pharmacology. His research effort is to investigate the role of a group of local anesthetics related to procaine as agents in restoring the deformability of irreversibly sickled cells. Exploration of the binding of the local anesthetics to normal and sickled erythrocyte membranes will provide information about the similarities and differences of local anesthetic binding sites in erythrocyte membranes as compared to axonal and synaptic membranes.

- MICHAEL W. LOES, University of Minnesota, has finished three years of medical school. His principal advisor is Bernard L. Mirkin, Ph.D., M.D., Director, Division of Clinical Pharmacology. He will participate in a study of digitalis intoxication in infants and children focusing on the relationship of serum and salivary digoxin levels to serum, erythrocyte and salivary electrolytes. Pre-clinical investigations have already been carried out and data on the fractional urinary clearance of digoxin from mongrel puppies, ranging in age from 1-28 days, and adult dogs have been gathered.

A clinical study investigating the kinetics of digoxin absorption and the relation of serum digoxin levels to cardiac arrhythmias in children has also been carried out in the Division. These data did not reveal any clear relationship between the onset or persistence of cardiac arrhythmias and serum digoxin levels. Consequently, serum levels alone appear to possess limited diagnostic potential for clearly identifying digoxin intoxication in young infants.

The objectives of the present study will determine:

- (1) Dose-response relationships between quantity of digoxin administered, the serum and salivary levels developed, the alteration in serum, erythrocyte and salivary electrolytes and changes in the EKG; and (2) the correlation of clinical drug intoxication with these parameters.

- **MICHAEL J. SCHWARZ**, Case Western Reserve University, has finished two years of medical school. His principal advisor is W. Leigh Thompson, Ph.D., M.D., Director, Clinical Pharmacology Program, Associate Professor of Medicine and Pharmacology, Department of Medicine. His research project will attempt to determine the effects of diuresis, tubular lumen pH, and renal perfusion altered singly and in combination on the renal clearance of a group of test drugs which have been chosen for their differences in volume and distribution pKa, lipid solubility, protein binding, extent of metabolism and rate of renal clearance. The aim is to study the relative effects on the renal clearance of these test barbiturates of inhibition of sodium and water reabsorption by mannitol, tromethamine and furosemide. In addition, the project will compare the relative effects on the renal clearance of these three barbiturates of urine alkalization by tromethamine, sodium bicarbonate alone and in combination with acetazolamide. Also, the attempt will be made to establish the relationships of varying doses of dopamine, PGA₁ and ethyl adenosine-5'-carboxylate, separately and in combination, to total renal perfusion, the regional distribution of blood flow within the kidney, and the clearance of the three test barbiturates. Further, it will establish the most effective safe means of increasing the renal clearance of three representative test drugs by simultaneous inhibition of sodium and water reabsorption, increasing urine pH, and augmenting renal perfusion.

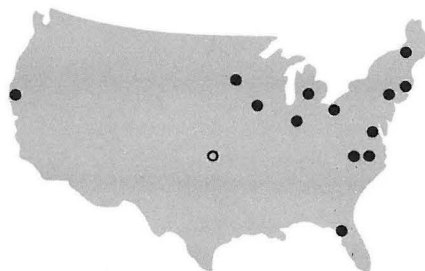
- **LLOYD M. STOOLMAN**, University of California, has finished all but his final year in medical school. His principal advisor is Kenneth L. Melmon, M.D., Chief, Division of Clinical Pharmacology. During the fellowship, Mr. Stoolman will participate in the study of the mechanism of tachyphylaxis in isolated S49 mouse lymphoma cells and its relationship to receptor availability for betamimetic amines. Work in the laboratory to date has demonstrated that (1) cells refractory to isoproterenol lose 25-50% of their functional beta adrenergic receptors; (2) phosphodiesterase, the primary cyclic AMP cleaving enzyme, is not critical to the expression of any aspect of tachyphylaxis; and (3) refractoriness to isoproterenol does not alter the response to agents which stimulate cyclase and intracellular cyclic AMP accumulation via binding at sites other than the beta adrenergic receptor. The implication of this conclusion is that isoproterenol may induce refractoriness to itself by decreasing the number of functional beta adrenergic receptors at the surface.

Mr. Stoolman's project will involve further tests and definition of this hypothesis.

- **ERIK R. SWENSON**, University of Florida, has completed two years of medical school. His principal advisor is Thomas H. Maren, M.D., Professor and Chairman, Department of

Pharmacology and Therapeutics. His research efforts will be directed toward the study of chemistry, physiology and inhibition of the Bohr Effect. The effort will examine the relationship and interaction between carbonic anhydrase and hemoglobin in the red cell. Other studies have shown that carbonic anhydrase inhibitors, such as acetazolamide, inhibit the rapid loading and unloading of that amount of oxygen which is transferred by the action of acid upon hemoglobin. Inhibition of carbonic anhydrase results in a hundredfold decrease in the rate of the Bohr shift. This finding would suggest that there is a virtual abolishment of the Bohr Effect in the physiological state following inhibition. Why carbonic anhydrase inhibition causes a marked reduction in the velocity of the Bohr shift has not been answered. In order to elucidate the role of the enzyme it will be necessary to examine the relation between the rate of the Bohr Effect and the rates of CO_2 hydration and HCO_3 dehydration in the absence and presence of carbonic anhydrase. Studies using an inhibitor will provide a means by which any degree of inhibition can be measured for its effects on the Bohr shift. It will be possible in this manner to determine where the rate limiting step lies in the Bohr shift and why carbonic anhydrase appears to be necessary for the generation of the Bohr shift.

• JAMES S. TIEDEMAN, Ph.D., Duke University, has finished two years of medical school. His principal advisor is Harold C. Strauss, M.D., Assistant Professor of Medicine and Pharmacology, Department of Medicine. His research effort will include both laboratory studies and clinical studies of the identification of the mechanisms of action of cardioactive agents. The studies will include continuing evaluation of the pharmacologic effects of disopyramide on sinus and atrioventricular nodal function in humans and on atrial arrhythmias. In addition, the project will examine the effects of several cardioactive agents in the rhythmic activity of cardiac Purkinje fibers using standard microelectrode techniques and isolated preparations of cardiac tissues.



Geographical distribution of Foundation "Medical Student Research Fellowships in Pharmacology-Clinical Pharmacology" program, 1974-1976

• One

○ More than One

The six students whose fellowships ended June, 1976 are:

- JONATHAN A. COHN, Rockefeller University. His principal supervisor was Attallah Kappas, M.D., Physician-in-Chief, Rockefeller Institute.
- DANIEL K. DAY, University of Iowa. His principal supervisor was Robert J. Roberts, M.D., Ph.D., Professor, Departments of Pharmacology and Pediatrics.
- JAMES M. HORTON, Duke University. Mr. Horton took part of his work at Duke University and at the University of Chicago. Mr. Horton moved to the University of Chicago when his principal supervisor, Robert B. Gunn, M.D., Associate Professor of Pharmacological and Physiological Sciences, moved to that University.
- WADE H. MARTIN, University of Kansas. His principal supervisor was Daniel L. Azarnoff, M.D., Distinguished Professor of Medicine and Pharmacology.
- ALAN L. NEESE, University of Vermont. His principal supervisor was Lester F. Soyka, M.D., Professor of Pharmacology and Pediatrics.
- ALAN J. RAVITZ, Michigan State University. His principal supervisors were Dr. J. Meites, Professor of Physiology and Dr. K. E. Moore, Professor of Pharmacology.

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. They provide salary and fringe benefits at levels which are expected to be consistent within the applicant university. The total number of awards made to date is thirteen.

FACULTY DEVELOPMENT AWARDS IN BASIC PHARMACOLOGY

Those who received awards beginning July 1, 1977 are:



R. Adron Harris,
Ph. D.

• R. ADRON HARRIS, Ph.D., Assistant Professor, Department of Pharmacology, School of Medicine, University of Missouri. This research program involves the use of behavioral and neurochemical techniques to study the mechanisms by which drugs such as ethanol, barbiturates and marijuana produce intoxication after acute administration and tolerance and physical dependence after chronic administration. The portion of the program dealing with behavioral evaluation of these drugs will utilize schedule-controlled (operant) behavior to compare and contrast the acute intoxication produced by various alcohols, barbiturates and cannabinoids (the active components of marijuana) and to compare the characteristics of the tolerance and physical dependence produced by chronic administration of these drugs. Other studies will attempt to relate these behavioral effects to neurochemical alterations. The long-range goal of this research program is to gain an understanding of the mechanisms by which these drugs produce their acute intoxicating effects as well as an understanding of the adaptive mechanisms by which chronic drug administration produces tolerance and physical dependence.



Michael E.
Maguire, Ph.D.

• MICHAEL E. MAGUIRE, Ph.D., Assistant Professor, Department of Pharmacology, School of Medicine, Case Western Reserve University. His research efforts have three objectives: (1) to study the metabolism of guanyl nucleotides during hormonal stimulation; conversely; (2) to determine how changes in the intracellular concentration of guanyl nucleotides affect response to hormonal agents; and (3) to delineate the tissue and hormonal specificity of guanyl nucleotides effects on hormone binding to membrane receptors.

Those who began their award in July, 1976 are:

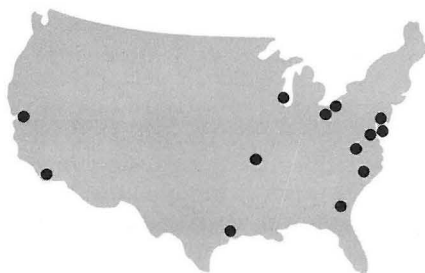
- SUE PIPER DUCKLES, Ph.D., Assistant Professor in Residence, Department of Pharmacology, School of Medicine, University of California.
- GARRETT J. GROSS, Ph.D., Assistant Professor, Department of Pharmacology, Medical College of Wisconsin.
- DANIEL A. KOECHEL, Ph.D., Assistant Professor, Department of Pharmacology and Therapeutics, Medical College of Ohio.

Those who entered the second year of their award in July, 1976 are:

- CARL L. JOHNSON, Ph.D., Associate Professor, Department of Pharmacology and Therapeutics, University of Cincinnati Medical Center.
- CLAIRE M. LATHERS, Ph.D., Assistant Professor, Department of Pharmacology, Medical College of Pennsylvania.

Those who ended their award in June, 1976 are:

- ING KANG HO, Ph.D., Associate Professor, Department of Pharmacology and Toxicology, University of Mississippi Medical Center.
- MICHAEL G. MAWHINNEY, Ph.D., Associate Professor, Departments of Pharmacology and Urology, School of Medicine, West Virginia University.
- SAMUEL J. STRADA, Ph.D., Associate Professor, Department of Pharmacology, The University of Texas Medical School.



Geographical distribution of
Foundation "Faculty
Development Awards in
Pharmacology" program,
1973-1977

• One

Pharmacology-Morphology: The aim of this program of Fellowship Awards 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 tissues and cellular structure.

The awards are for 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, 33 awards have been made.

The program requires that a 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 disciplinary approach by using his primary discipline as a medium for acquiring the second.

FELLOWSHIP AWARDS IN PHARMACOLOGY-MORPHOLOGY

The recipients of fellowships which began in July, 1976 are:



Cheryl F. Dreyfus,
Ph. D.

- CHERYL F. DREYFUS, Ph.D., Staff Associate, Department of Anatomy, College of Physicians and Surgeons, Columbia University. Dr. Dreyfus will attempt to determine whether and how neurons recognize their appropriate target neurons so that a growing axon can find the proper cell with which to establish synaptic contact. They will be grown in tissue culture. The aminergic neurons will be co-cultured with regions of the central nervous system which have been: (1) heavily innervated by aminergic fibers; or (2) not innervated by aminergic fibers. The growing neurons will thus have a choice to establish relationships with an appropriate or a non-appropriate region. Neurochemical, histofluorescent and neurophysiologic methods will be used to determine whether connections are established and whether, if they are, these are functional.



Susan B. Stearns,
Ph. D.

- SUSAN B. STEARNS, Ph.D., Postdoctoral Fellow, Department of Pharmacology, Upstate Medical Center, State University of New York. Dr. Stearns plans to investigate certain aspects of diabetes by studies on two experimental animal models whose disease resembles that found in the human. One model is the genetically diabetic mouse, the other is the mouse made diabetic by injection of the drug streptozotocin which destroys insulin producing cells in the pancreas. Dr. Stearns will examine heart and skeletal muscle from these mice to characterize the development of the diabetic state as it influences the structure of these tissues and

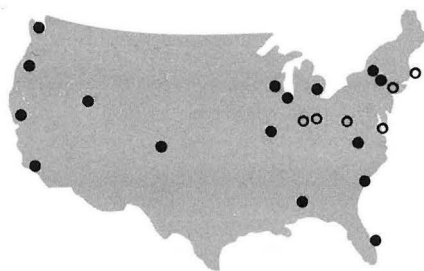
their ability to respond to insulin by synthesizing glycogen. The results of these studies should increase understanding of muscle metabolism in diabetes as well as the development of the disease.

Those individuals who entered the second year of their fellowships in July, 1976 are:

- CLARA F. ASNES, Ph.D., Postdoctoral Fellow, Department of Biological Sciences, University of California.
- RAYMOND J. DINGLEDINE, Ph.D., Postdoctoral Fellow, Addiction Research Foundation, Palo Alto, California. Dr. Dingleline is using his fellowship at the MRC Neurochemical Pharmacology Unit, University of Cambridge.
- JOHN W. MILLS, Ph.D., Assistant in Biology, Department of Renal Biophysics, Massachusetts General Hospital.
- R. WILLIAM SOLLER, Ph.D., Instructor in Pharmacology, Department of Pharmacology, School of Medicine, University of Pennsylvania.

Those individuals whose fellowships concluded in June, 1976 are:

- JOHN I. CLARK, Ph.D., Postdoctoral Fellow, Department of Anatomy, Harvard Medical School.
- JANET D. SMITH, Ph.D., Assistant Professor, Department of Anatomy, The Medical College of Pennsylvania.

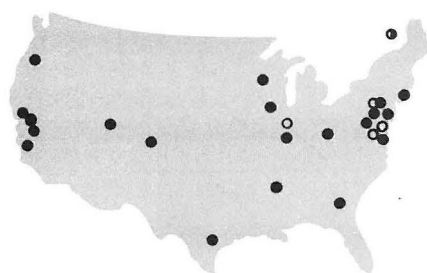


Geographical distribution of Foundation "Fellowship Awards in Pharmacology-Morphology," 1968-1976

- One
- More than one

RESEARCH GRANTS

An important aspect of PMA Foundation effort has been the support of fundamental research in drug toxicology. Between 1966 and the end of 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, into less research. The Foundation does, however, continue to accept requests for support and suggestions for pertinent research projects, since it is important that the potential for helping that particularly promising effort within the Foundation be maintained.



Geographical distribution of
Foundation general research
grants, 1966-1977

- One
- More than One
- ◉ Outside U. S.

RESEARCH STARTER GRANTS

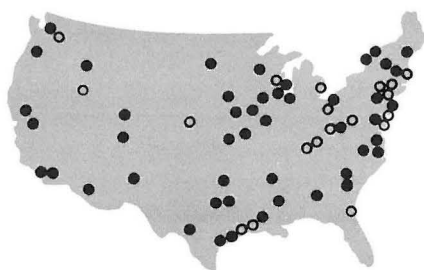
As part of the change of emphasis in 1971 which sought to direct monies more toward the development of the individual, a program of Research Starter Grants was initiated. These grants are intended to provide financial support for beginning investigators. The program currently offers \$5,000 a year for two years, with the second year contingent upon a continuing need for the funds. Beginning with the new awards starting in January, 1978, the yearly grant will increase to \$6,000. The research areas of interest within this program are in pharmacology, clinical pharmacology and drug toxicology. The program allows for approximately 20 research grants each year. The first awards were made in 1972. A total of 142 research starter grants have been made, including the 24 awards beginning January 1, 1977.

The recipients of the grants beginning January, 1977 are:

- | | |
|--|--|
| REBECCA J. ANDERSON, Ph.D.
The George Washington University
School of Medicine | MARK JAE REASOR, Ph.D.
West Virginia University
Medical Center |
| CRAIG W. BEATTIE, Ph.D.
Wake Forest University
Bowman Gray School of Medicine | HELEN J. ROSE, M.D.
Emory University
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School of Medicine | |
| LUC M. V. HONDEGHEM, M.D., Ph.D.
University of California
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College of Pharmacy | |
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St. Jude Children's Research Hospital | |
| DANIEL G. PACE, Ph.D.
Case Western Reserve University
School of Medicine | |
| JAMES R. POWELL, Ph.D.
Emory University
School of Medicine | |

Review of the need of the 27 research starter grantees whose awards began January 1, 1976 for a second year of the awards resulted in 23 of them having their awards continued. These are:

DANIEL ACOSTA, JR., Ph.D. University of Texas College of Pharmacy (Austin)	JAMES M. ROBERTS, M.D. University of California School of Medicine (San Francisco)
WILLIAM T. BECK, Ph.D. St. Jude Children's Research Hospital	DANNY DAH-YING SHEN, Ph.D. University of Kansas Medical Center
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RAYMOND M. QUOCK, Ph.D. University of the Pacific School of Pharmacy	



Geographical distribution of Foundation awards under the "Research Starter Grants" program, 1972-1977

- One
- More than One

PUBLICATIONS AND OTHER GRANT SUPPORT

A grant of \$10,205 was made to the American Society for Pharmacology and Experimental Therapeutics to update the career brochure "This is the Profession of Pharmacology." This brochure is the principal information document on opportunities in pharmacology.

A grant of \$3,000 was made to William Y. W. Au, M.D., Professor of Pharmacology and Medicine, University of Arkansas for Medical Sciences, to help implement certain programs and services within this newly developed unit.

FOUNDATION FINANCES

THE TOTAL INCOME OF THE FOUNDATION in 1976 was \$975,664. Of this amount, \$885,748 came from contributions. The balance of \$90,916 came from investments and refunds of unexpended balances from grants.

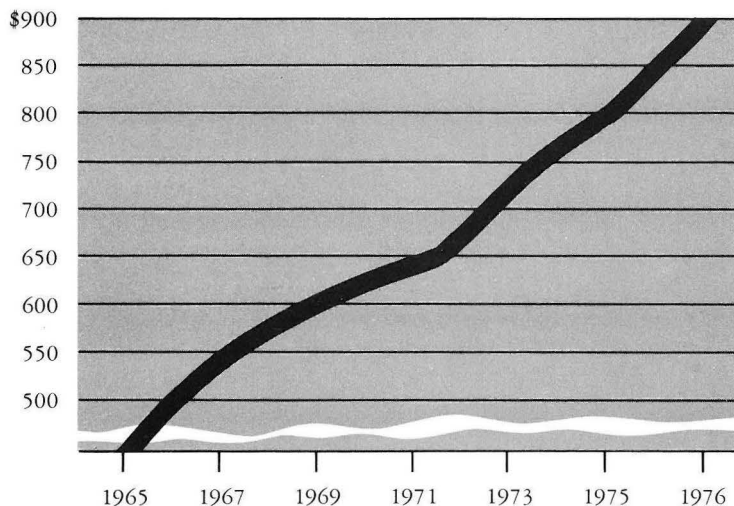
Contributions were received from approximately three out of every four PMA Member Firms. Contributions were also received during 1976 from individuals and other groups in the health field.

Grants, Foundation-sponsored programs and other expenses for 1976 amounted to \$792,930. Of this total, \$650,597 represented expenditures for grants and Foundation-sponsored programs. There was a fund balance of \$1,409,408 as of December 31, 1976. 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 distributed. As of December 31, 1976, the contingency liability for 1977 was approximately \$622,000.

Financial Report. The Foundation's financial position as of December 31, 1976 has been audited by the accounting firm of Ernst & Ernst. Copies of this statement will be supplied upon request.

Financial statements have been issued to contributors quarterly during 1976. These reports are prepared by Washington, D. C. accounting firm of Buchanan & Company.

PMA Foundation
Contribution Income
1965-1976 (Thousands)



Statement of Income and Expenditures
For the year ended December 31, 1976

Income

Contributions — Note a	\$ 885,748
Income from Investments	76,392
Miscellaneous Income	13,524
TOTAL INCOME	\$ 975,664

Expenditures

Grants — Note b

Clinical Pharmacology Faculty Awards	\$ 192,325
Clinical Pharmacology Fellowships	34,702
Basic Pharmacology Faculty Awards	115,315
Medical Student Research Fellowships	28,350
Pharmacology-Morphology Fellowships	71,700
Research Starter Grants	195,000
American Society for Pharmacology and Experimental Therapeutics	10,205
University of Chicago	3,000
	\$ 650,597

Administrative and Special Meeting Expenses	142,333
TOTAL EXPENDITURES	\$ 792,930

Excess of income over expenditures	\$ 182,734
Fund balance at January 1, 1976	\$1,226,674
Fund balance at December 31, 1976	\$1,409,408

Note a—The Foundation received contributions of \$87,500 prior to December 31, 1976 which the Foundation considered applicable to 1977 and, therefore, are not recorded as income in 1976.

Note b—In addition to the amounts shown, the Foundation has committed itself, subject to annual review, to make certain grants. At December 31, 1976 the amounts still to be disbursed with respect to these grants during 1977 amounted to approximately \$622,000.

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 agreed to initially, and which still govern the distribution of funds, are support of fundamental research in drug toxicology, and the support of programs of research and training for personnel in clinical pharmacology and drug evaluation.

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 which 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 18.

In line with this change of emphasis, the Foundation is expanding support within its current educational program 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.

ORGANIZATION AND ADMINISTRATION



Daniel C. Searle



C. Joseph Stetler



Thomas E.
Hanrahan

THE PMA FOUNDATION OPERATES THROUGH its officers and four advisory committees. The Chairman of the Board is Daniel C. Searle, Chairman of the Board, G. D. Searle & Co., C. Joseph Stetler is President, Thomas E. Hanrahan is Executive Director and I. C. Winter, M.D., Ph.D. serves as staff consultant. In August, 1976 Mr. Searle was reelected Chairman of the Board. W. Clarke Wescoe, M.D., Chairman of the Board and Chief Executive Officer, Sterling Drug, Inc. was reelected Vice Chairman and Donald van Roden, President, Smith Kline & French Laboratories, was reelected Secretary, Treasurer.

In reaching decisions on the most worthwhile activities for support, the Board of Directors has had the advice of extremely knowledgeable individuals serving on four advisory committees.

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² Resigned May, 1976

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³ Resigned June, 1976

⁴ Resigned May, 1976

⁵ Resigned April, 1976

⁶ New Member June, 1976

⁷ New Member August, 1976

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⁹ Resigned March, 1976

¹⁰ New Member February, 1977

¹¹ Resigned January, 1977

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¹² New Member January, 1977

¹³ Member Until December, 1976

¹⁴ Deceased July, 1976

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¹⁵ Deceased May, 1977

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APPLICATIONS

THE FOUNDATION ACCEPTS REQUESTS FOR support and suggestions for pertinent research projects from qualified institutions and individuals. However, in 1971 the Foundation underwent a major shift in program direction, now emphasizing education and training support.

To expedite the handling of requests for research support, it is suggested that a brief one or two page letter be directed to the Foundation, outlining the intended project and an estimate of the funds involved. After review of this more informal request by members of the Scientific Advisory Committee to determine the degree of likelihood of the project falling within Foundation guidelines, a decision can be made as to whether a formal proposal is warranted.

Letters should be addressed to:

Thomas E. Hanrahan
Executive Director
Pharmaceutical Manufacturers
Association Foundation, Inc.
1155 15th Street, N.W.
Washington, D. C. 20005

PHARMACEUTICAL MANUFACTURERS
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