Pharmaceutical Manufacturers Association Foundation, Inc.
1968 Annual Report


INVOLVEMENT
'68

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Become involved! From how many settings, how many times and in how many different ways did you receive this urging during 1968? "Commitment," "community action," "local involvement," "dialogue", are among the key words and phrases so often voiced by those seeking to arouse others to action. A number of social, political, economic and religious concerns provided the issues. National and local meetings, as well as the streets and sidewalks of this country, provided the forums.

In an analogous fashion, 1968 witnessed involvement by the PMA Foundation with the scientific community at an increasing tempo. *Dialogue* through support of meetings, continuing *commitment* to support of research, *local involvement* by various institutions in the Foundation's educational programs, and *community action* through concerted efforts by representatives of the government, academia, and industry, characterize 1968 for the PMA Foundation.

What began in 1965, continued in a small way in 1966, and grew to such a degree in 1967 that the PMA Foundation could present itself as a firmly established scientific organization committed to the support of imaginative programs, has in 1968 become increasingly involved in a very real sense, within the scientific arena.

This report reflects the variety of activities supported by the PMA Foundation. None of this record of achievement would be possible without the further involvement of three groups—the Foundation's advisory committees to the Board of Directors, its many financial contributors, and those individuals who submitted the many well conceived applications for consideration. To these three groups, the Board of Directors extends a sincere expression of thanks.

activities

Over $1.8 million has been authorized to date by the PMA Foundation for a variety of workshops, conferences, research and educational programs. The Foundation has reached across the entire United States with these programs. This section presents the highlights of the various efforts the Foundation has supported during the year.

Workshops and Conferences

Workshops and conferences are important educational efforts and have continued to receive support. Programs scheduled for 1968 and authorized in 1967 included a third workshop on drug metabolism held June 24-28, 1968, at the University of California, San Francisco Medical Center, and a conference on high resolution autoradiography of diffusible substances held June 2-4, 1968, at the University of Chicago. Meetings and other activities approved for support in 1968, plus a status report and a grant to the American Society of Pharmacology and Experimental Therapeutics for support of special summer courses in pharmacology are described below.

Drug Metabolism. *An amount of $20,000 has been authorized for the preparation of a book entitled "Fundamentals of Drug Metabolism and Disposition."* Three workshops on drug metabolism supported by the PMA Foundation have been described in previous Annual Reports. Wider availability of the information presented at these workshops will be possible as a result of this new publication. The editors of the book are the directors of the three workshops, Drs. Bert N. La Du, New York University; H. George Mandel, George Washington University; and E. Leong Way, University of California, San Francisco. The Foundation is cooperating with the National Academy of Sciences' Drug Research Board in this effort.

The book will provide in one volume a basic understanding of drug metabolism, a compilation of information which does not now exist.

Support of $10,000 was provided for a "Conference on Application of Newer Physical Techniques to the Study of Drug Metabolism," held June 12-14, 1968 at the National Bureau of Standards in Gaithersburg, Maryland. The meeting was co-sponsored with the Foundation by the National Institute of General Medical Sciences—National Institutes of Health, the National Academy of Sciences' Drug Research Board, and the National Bureau of Standards. The purpose was to familiarize the nearly 400 scientists who attended with the potential and limitations of the newer physical techniques developed for the study of the metabolism of foreign substances. With emphasis on the biological applications of these techniques, the conference was unique among the many other programs which have been concerned with newer methods of instrument technology.

Dr. Gilbert Mannering, University of Minnesota, delivering opening remarks as chairman of the "Conference on Application of Newer Physical Techniques to the Study of Drug Metabolism."

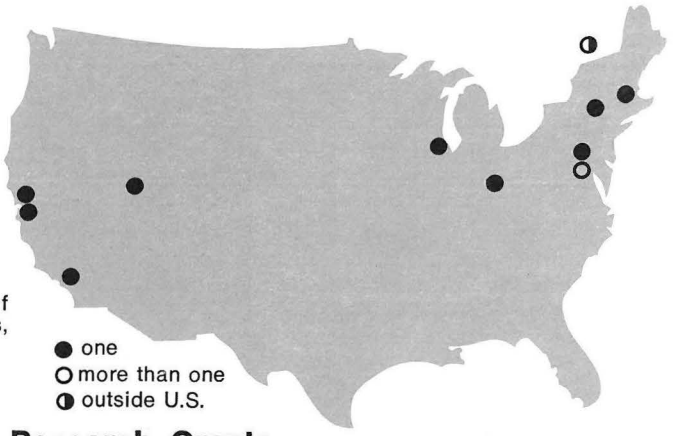
Pharmacology—Clinical Pharmacology. Scheduled to begin in the summer of 1969 is a series of summer sessions conducted by the American Society of Pharmacology and Experimental Therapeutics (ASPET) for graduate students in pharmacology. An award of $176,880 for the four-year project was made by the Foundation in 1967 for these four to six-week courses in advanced pharmacology for Ph.D. candidates and will be offered at various universities selected because of specialization in selected fields. Up to 50 doctoral candidates can be accommodated at each session.

The purpose of the program is to overcome a basic problem in pharmacological education. Many pharmacology departments are not large enough to provide teaching in all major research areas and teaching interests, and graduate students in these institutions may not be fully aware of some of the other major problems in pharmacology. Through these summer programs, it is hoped that broader exposure will give the graduate student a better perspective as he continues his career in pharmacology.

The University of Minnesota, Department of Pharmacology, is the host institution for the 1969 summer session. The course will deal with drug metabolism and biochemical pharmacology. The director is Gilbert Mannering, Ph.D., Professor of Pharmacology.

Universities involved for the next three years of the program are:

- Columbia University, Department of Pharmacology—host for 1970. The course will deal with cardiovascular pharmacology.
- The University of California, San Francisco, Department of Pharmacology—host for 1971. The course will deal with neuropharmacology and mechanisms of drug action.
- Vanderbilt University, Department of Pharmacology—host for 1972. The course will deal with psychopharmacology.



Geographic distribution of Foundation research grants, 1966-1968.

Research Grants

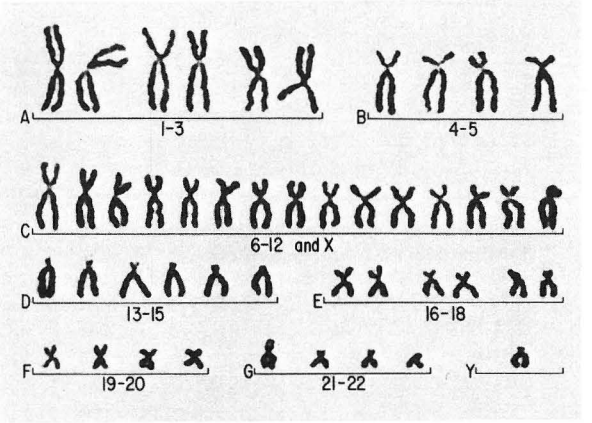
A second aspect of the Foundation's activities is support of fundamental research in drug toxicology. Since 1966, 12 research grants have been made by the Foundation. Support has expired on two grants. The other ten grants are scheduled to continue for varying periods of time, extending through 1971.

In 1968, new grants were made to four institutions. They are: University of Montreal, Department of Pharmacology, Montreal, Quebec, Canada; University of Chicago, Department of Obstetrics-Gynecology, Chicago, Illinois; Johns Hopkins University, Department of Pediatrics, Baltimore, Maryland; and the University of California, Department of Medicine, San Francisco, California.

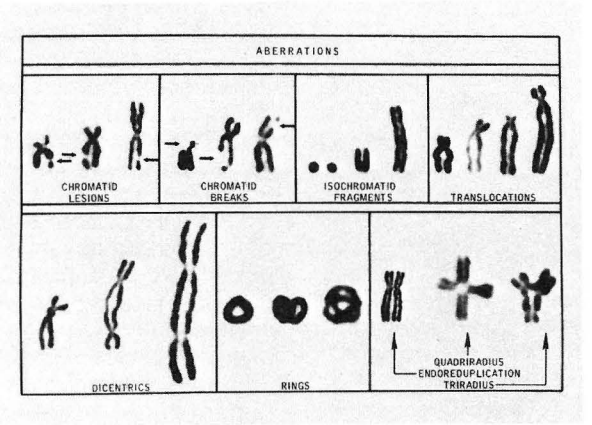
Six awards made in 1967 which continued into 1968 were made to: Georgetown University, Renal and Electrolyte Division, Washington, D.C.; Albany Medical College of Union University, Institute of Experimental Pathology and Toxicology, Albany, New York; University of Southern California, Department of Medicine, Los Angeles, California; Registry of Tissue Reactions to Drugs, Armed Forces Institute of Pathology, Washington, D.C.; University of Utah, Department of Pediatrics, Salt Lake City, Utah; and the Institute for Developmental Research, Children's Hospital Research Foundation, University of Cincinnati, Cincinnati, Ohio.

The ten current research grants fall into the following categories:

Animal-Human Predictability Studies. *A grant of $68,549 for a two-year period beginning January 20, 1969, was made to the Department of Obstetrics and Gynecology, Chicago Lying-In Hospital, Pritzker School of Medicine, University of Chicago.* The principal investigator is Anthony P. Amarose, Ph.D., and co-investigator is James L. Burks, M.D., both Assistant Professors in the Department of Obstetrics and Gynecology. The funds will support studies to establish an experimental animal system to assist in ascertaining whether a relationship exists between chromosome damage



This is a representative complement of 46 chromosomes from a cultured lymphocyte obtained from a normal human male. The chromosomes consist of 22 equal pairs and one unequal pair (one X sex chromosome and one Y sex chromosome.)

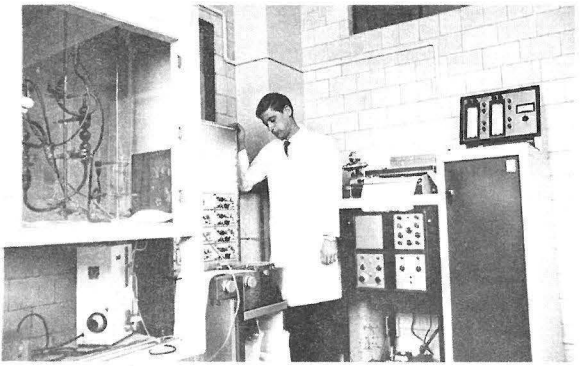


This figure is a compilation of the more commonly seen types of chromosome aberrations.

and drug intake. Chromosomes, threadlike structures in the nucleus of a cell, carry the hereditary elements that enable living beings to reproduce. This study will measure the response in the chromosomes of lymphocytes (a form of the white blood cell) and bone marrow cells to drug stimuli.

A grant totaling $26,000 over a two-year period beginning September 1, 1968, has been made to Gabriel L. Plaa, Ph.D., Professor and Chairman, Department of Pharmacology, School of Medicine, University of Montreal. This is the first research award made by the Foundation outside the United States and will support a number of studies dealing with the production of intrahepatic cholestasis, a reaction characterized by the development of jaundice and changes in the liver function which can occur in susceptible individuals following treatment with certain drugs.

The overall goal is to develop an experimental animal system which can be employed to detect intrahepatic cholestasis in the investigational stage of drug development. The project will involve the study of the production of this reaction using several types of chem-



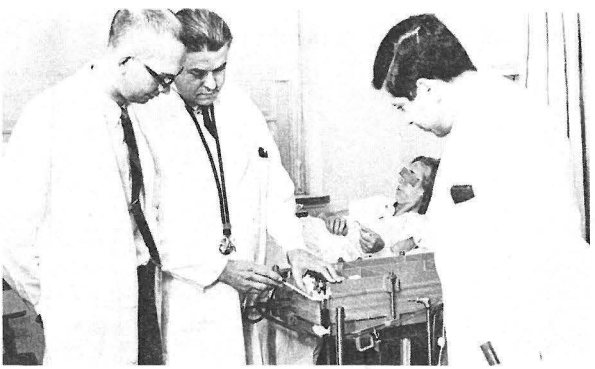
Perfused liver apparatus (left) and gas chromatograph (right) used in studying the effects of chemicals on liver function.

ical agents in several species of animals. Changes in the liver function will be correlated with changes in liver structure.

Dialyzable Drugs. A grant of $20,000 per year for up to five years, for a total of $100,000, beginning January 1, 1967, to the Renal and Electrolyte Division, Georgetown University Hospital, completed its second year during 1968. George E. Schreiner, M.D., Professor of Medicine and Director, Renal and Electrolyte Division, is the principal investigator. The award has been used to support research relating to the hemodialysis of drugs and poisons and a registry of dialysis findings, developed in cooperation with the American Society of Artificial Internal Organs. Hemodialysis is the removal of certain elements (in this case drugs) from the blood by diffusion through a semi-permeable membrane. The artificial kidney utilizes this procedure.

In 1967, the research group prepared and published a review of the dialysis of poisons and drugs which appeared in the *Transactions of the American Society of Artificial Internal Organs,* Volume XIII, pages 369-393. Clinical reports which provided the basis for this review were received from 120 ASAIO members representing 106 different medical institutions. This review contains 322 significant references.

In 1968, a further review of dialyzable drugs and poisons was published in the *Transactions of the American Society of Artificial Internal Organs,* Volume XIV, pages 440-453.



Drs. George E. Schreiner (center), Gerald J. Rutecki (left), and Larry Siegel viewing an artificial kidney machine in connection with dialysis of poisons at the Georgetown University Hospital.

Drug-Related Structural Studies. A grant of $25,000 a year for a four-year period, for a total of $100,000, beginning August 1, 1967, to the Institute of Experimental Pathology and Toxicology of the Albany Medical College of Union University, Albany, New York, entered its second year in 1968. The principal investigator is Frederick Coulston, Ph.D., Director of the Institute. The first year's funds have accelerated the Institute's program of studies of the relation of structural changes in the subcellular organelles of important tissues to the actions of chemicals and drugs on various functional properties of these tissues. During the year, studies have concentrated on the correlation of morphologic changes determined by light microscopy, histochemistry and electron microscopy with the biochemical changes in tissues following acute and chronic administration of various pesticides.

Drug Surveillance. *A grant of $48,000 was made for* a two-year period beginning January 1, 1968, to the *University of Southern California for partial support of a study of adverse reactions to drugs at the Los Angeles County General Hospital.* The program, under the direction of Robert F. Maronde, M.D., Associate Professor of Pharmacology and Medicine, is part of a larger project composed of two parts: an adverse drug reaction study of hospitalized patients, and an inquiry into drug ordering and dispensing for outpatients.

Involved in the adverse drug reaction reporting phase of the study are approximately 20,000 patients who are admitted yearly to the medical ward in the Los Angeles County General Hospital.

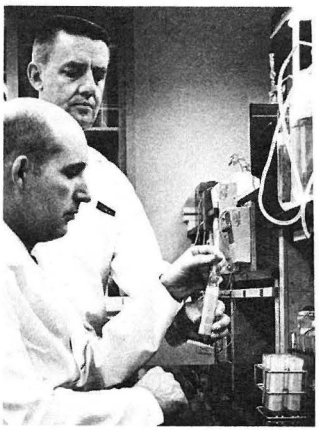
Much effort in 1968 has been devoted to the development of appropriate computer programs. During the year, members of the physician surveillance team have been retained. These physicians will note significant patient events and other circumstances outside the specific areas of recognizable side effects of a drug. A nurse monitoring team is also involved in the study to record similar information. The use of the two different surveillance teams will provide an opportunity to evaluate the relative merits of the two approaches within the one study.

A member of the physician surveillance team operating the IBM 1092-93 terminal which is part of the computer system used in the Los Angeles County General Hospital drug surveillance program.

The information to be computerized includes the necessary patient identification, diet orders, drug orders, the nurses' monitoring data, diagnosis, laboratory scheduling of routine screening of laboratory tests, and the laboratory results. The present schedule calls for the further development of computer programs necessary to the analysis of the data and beginning of the analysis of the patient data during 1969.

A grant of $27,225 was made to Universities Associated for Research and Education in Pathology to continue support in 1968 of the Registry of Tissue Reactions to Drugs, Armed Forces Institute of Pathology, Washington, D.C., for its third year of operation. The Registry is co-sponsored and equally supported with the Foundation by the American Medical Association, the Food and Drug Administration, and the National Institutes of Health. Nelson S. Irey, M.D., is the Registrar. The Registry obtains biopsy and autopsy tissue specimens on a voluntary basis from the participating organizations and from pathologists in practice who suspect drug reaction cases. The Registry subjects these specimens to microscopic examination and reports its findings to the referring pathologists. As of the end of 1968, the Registry has accession to a total of 1,038 cases in the active file with nearly 9,000 cases available in the reserve files of the other registries maintained by the Armed Forces Institute of Pathology.

The Registry continues to serve an educational function. Three parts of a syllabus entitled "Diagnostic Problems and Methods in Drug-Induced Diseases" have been prepared and are available with slides. These various parts of the syllabus contain descriptions of the methodology used by the Registry in specific cases and a variety of pathologic changes in tissues related to drugs.



Dr. Alan K. Done (standing) and technician, Arnold Peart, prepare an ultrafiltrate of serum to determine whether a drug competes with bilirubin for binding to serum proteins.

Fetal and Neonatal Pharmacology. *An award of $18,000 for an additional year on a grant which expired in 1968 was made to the Department of Pediatrics at the University of Utah, and Alan K. Done, M.D., Professor of Pediatrics,* for the study of the drug potentiation of kernicterus, a condition of hyperbilirubinemia associated with jaundice which may produce brain damage in the new born. It is potentiated by certain widely used drugs which compete with bilirubin for binding to serum albumin, thereby increasing the level of circulating free bilirubin. The Gunn rat, a special strain, which has an inherited inability to conjugate bilirubin, is being used as a test animal. The objective of the study is to develop a method by which drugs may be tested for their potential to produce kernicterus in the new born.

The work thus far has indicated that many of the *in vitro* procedures which have been used for measuring the ability of drugs to compete with bilirubin for protein-binding are unreliable and not consistent with *in vivo* findings in the Gunn rat. Therefore, data is

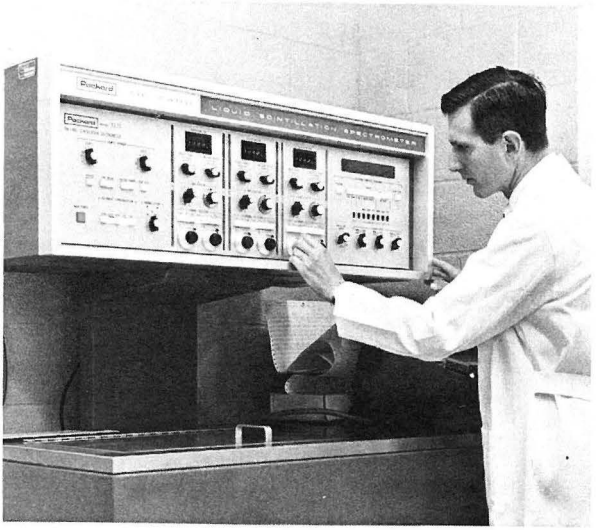
needed concerning the identity of sites for drug and bilirubin binding and, further, it must be shown that competition does indeed occur.

A grant of $50,000 a year for five years, for a total of $250,000, to Josef Warkany, M.D., Professor of Research Pediatrics, on behalf of the Children's Hospital Research Foundation beginning January 1, 1967, for partial support of the activities of the Division of Fetal Pharmacology of the Institute for Developmental Research completed its second year in 1968. The entire sixth floor of the Institute, which opened in June, 1968, is devoted to the activities of the Division and the funds are being used to provide staff and equipment for basic research. Ernest F. Zimmerman, M.D., assumed his duties as Director of the Division in June, 1968. Dr. Roger Ganschow, formerly at Stanford University, is his assistant.

Dr. James G. Wilson, Institute for Developmental Research, viewing the skeleton of a primate fetus.

The funds granted by the Foundation have been used also to stimulate research in fetal pharmacology within other divisions of the Institute. One such instance is a small amount of support to James G. Wilson, Ph.D., Director, Division of Pathologic Embryology. He is primarily concerned with the descriptive aspects of experimental teratology, and has become increasingly convinced that an urgent need exists for better understanding of the basic mechanisms that underlie abnormal development. He has enlisted the aid of a multidisciplinary group to continue efforts to localize the site of action of carbonic anhydrase inhibitors known to cause abnormal development in rats before a measurable amount of the enzyme can be demonstrated in the embryo. Dr. Wilson's work is done in cooperation with Dr. Herbert J. Schumacher of the Department of Environmental Health and Pharmacology, University of Cincinnati College of Medicine.

Dr. Ernest F. Zimmerman, Institute for Developmental Research, measuring radioactivity of RNA and proteins synthesized by developing organisms which may be affected by teratogenic agents.

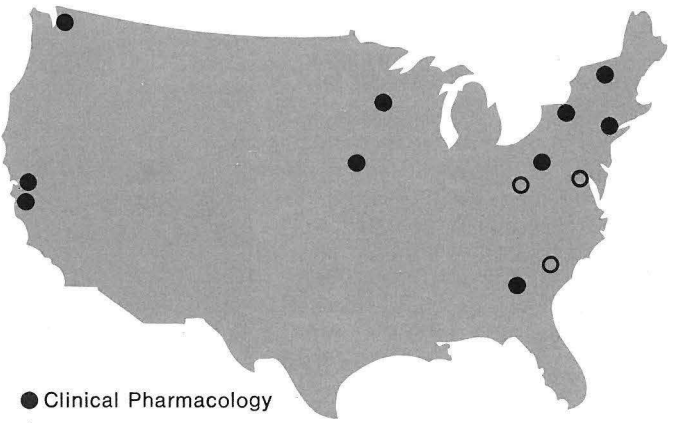


A grant of $50,000 for a two-year period beginning January 1, 1969, has been made to Robert E. Cooke, M.D., Given Foundation Professor of Pediatrics, the Johns Hopkins University School of Medicine, for basic and clinical research on the effects of drugs when given to the developing organism. This work will be done within a new unit devoted to developmental pharmacology within the Department of Pediatrics under the direction of Paul S. Lietman, M.D. Emphasis in the laboratory will be placed on pharmacologic-agents affecting protein synthesis and its regulation.

Pharmacokinetics. A grant of $9,400 was made to Kenneth L. Melmon, M.D., Chief, Division of Clinical Pharmacology, Department of Medicine, University of California, San Francisco Medical Center, to assist on a temporary basis a number of projects bringing together clinical pharmacologists with pharmacokinetics experts to probe a variety of areas of study of drugs and their distribution in man.

Education and Training Programs

To attain its objectives in the field of education, the Foundation has sponsored two unique programs in clinical pharmacology and one in the combined fields of pharmacology and pathology. In addition, a career promotion brochure for the field of pharmacology has been supported. The two clinical pharmacology programs, one with hoped-for immediate results, and the other more long-range, have provided opportunities for a number of individuals to extend their career commitments in the field of clinical pharmacology or to acquaint themselves with the techniques of this field of medicine. These education and training programs proved to be highly successful and much sought-after awards in 1968.



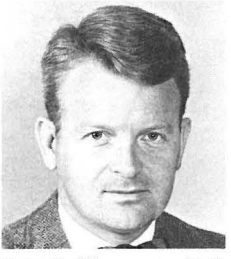
Geographic distribution of Foundation awards under the "Faculty Development Awards in Clinical Pharmacology" program, 1966-68; and Fellowship Awards in Pharmacologic-Pathology, 1968.

Clinical Pharmacology. Through the "Faculty Development Awards in Clinical Pharmacology" program, the Foundation makes two-year awards to medical schools for salary support of full-time junior faculty members. To best meet the needs of the applicant universities and the candidates they sponsor, the level of support is variable and it is aimed at keeping within the existing salary structure of the applicant university. The Board of Directors has established a yearly fund of $100,000 for this program.

With the awards made in 1968 scheduled to begin July 1, 1969, ten individuals have been supported under this program since 1967. In addition, a third year of support has been extended to John Holcenberg, M.D., University of Washington, Seattle. This third year of support was possible through a change in the program during 1968. As the experience with the program increased, it became apparent that the program can be strengthened by having a third year available in some situations.

Vincent S. Aoki, M.D.

Lester F. Soyka, M.D.



Pate D. Thomson, M.D.

Recipients of the new faculty awards beginning July 1, 1969 are:

- Vincent S. Aoki, M.D., Assistant Professor, Department of Internal Medicine and Pharmacology, College of Medicine, University of Iowa. Dr. Aoki, presently at the United States Army Research Institute of Developmental Medicine in Natick, Massachusetts, will rejoin the faculty of the University of Iowa. He plans to develop a program of investigation of the effects of drugs on the pulmonary vascular bed. He will work with Dr. William R. Wilson, Professor and Head of the Section of Clinical Pharmacology, and will play a major role in the teaching of clinical pharmacology to third and fourth year medical students. Additional responsibilities Dr. Aoki will have include the training of research fellows in the clinical pharmacology program.

- Lester F. Soyka, M.D., will serve as Assistant Professor of Pediatrics, Department of Pediatrics, School of Medicine, Stanford University. The award will enable Dr. Soyka to continue his preparation for a career in teaching and investigation in developmental pharmacology. This pediatric department has long been involved in research dealing with immaturity at the biochemical level and the Department of Pharmacology considers developmental studies as one of its principal areas of concern. Dr. Soyka's goal is to collaborate in establishment of a clinical pharmacology unit.

- Pate D. Thomson, M.D., as an Instructor in the Department of Medicine, School of Medicine, University of California, San Francisco Medical Center, will teach courses in basic and clinical pharmacology. In addition, he will participate in research to determine the effects of diseases on the pharmacokinetics of drugs used in their treatment. He will also attempt to define what other mechanisms are important determinants of drug distribution.

Stanley C. Ushinski, M.D.

• Stanley C. Ushinski, M.D., as Assistant Professor of Pediatrics and Pharmacology, School of Medicine, University of Pittsburgh, will work towards the organization of a Clinical Pharmacology Section in the Department of Pediatrics. He will expand his experience in experimental-analytic laboratory techniques with emphasis on the study of bronchial smooth muscle in "normal" and "allergenic" individuals.

Recipients of awards which began July 1, 1967, are:

• Faruk S. Abuzzahab, Sr., M.D., Assistant Professor, Department of Psychiatry and Pharmacology, University of Minnesota, is conducting research in both basic and clinical pharmacology.

• John S. Holcenberg, M.D., Assistant Professor, Division of Clinical Pharmacology, Department of Medicine, University of Washington, Seattle, is extending his training in biochemical approaches to clinical pharmacology.

• John L. McNay, M.D., Associate Professor of Medicine and Assistant Professor of Pharmacology, Emory University, is conducting research in renal physiology and pharmacology.

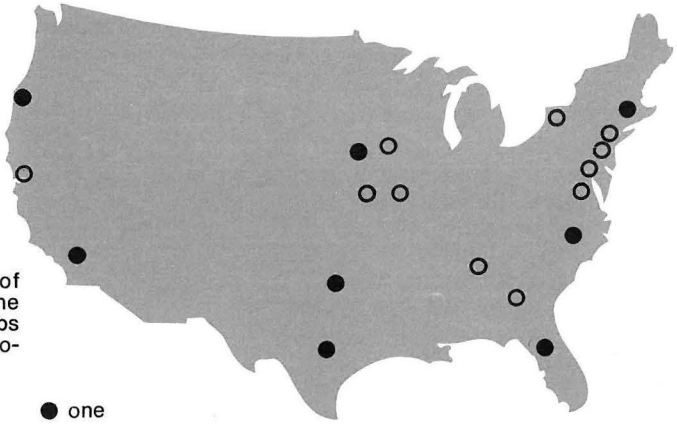
Recipients of awards which began July 1, 1968, are:

• William Y. W. Au, M.D., Assistant Professor of Pharmacology and Medicine, University of Rochester, is engaged in research on the effects of hormones and other agents affecting bone metabolism.

• Arthur H. Hayes, M.D., Assistant Professor of Pharmacology and Medicine, Cornell University Medical College, is furthering his training in the cardiovascular field.

• Donald S. Robinson, M.D., Assistant Professor of Medicine and Pharmacology, University of Vermont, is involved in studies in biochemical pharmacology.

"The Medical Student Traineeships in Clinical Pharmacology" program, offered for the first time in 1966, provides opportunities to medical students to become better acquainted with the basic techniques in the field of clinical pharmacology. A hoped-for long-range result is that some of these students may retain their interest in clinical pharmacology and choose this field as a career. The program provides $1,000 to each student for a three-month period in a clinical pharmacology unit, primarily concerned with research and training. A yearly fund of $20,000 has been authorized for this program. Since it was first offered in 1967, 40 medical students from 21 medical schools have participated in the program.



Geographic distribution of Foundation awards under the "Medical Student Traineeships in Clinical Pharmacology" program 1967-1968.

The universities and students receiving these awards in 1968 are:

University of California *on behalf of* Mr. James Waldman

Cornell University Medical College *on behalf of* Mr. William W. Goodhue, Jr.

Duke University *on behalf of* Miss Marcia A. Keleman

Emory University *on behalf of* Mr. Howard T. Brock, Jr. and Mr. Robert R. M. Gifford

University of Florida *on behalf of* Mr. Ronald Aronson

Georgetown University *on behalf of* Mr. Richard S. Kruse

Harvard Medical School *on behalf of* Mr. Dennis A. Ausiello

University of Iowa *on behalf of* Mr. Steven P. Combs and Mr. John D. Miller

University of Kansas *on behalf of* Mr. John P. Atkinson

University of Oklahoma *on behalf of* Mr. William Hamilton

University of Oregon *on behalf of* Mr. Albert D. Jacobsen

University of Rochester *on behalf of* Mr. Werner A. Bleyer and Mr. Charles M. Fogarty

Temple University *on behalf of* Mr. Larry E. Magargal.

University of Texas *on behalf of* Mr. Gregory L. Jenkins

Vanderbilt University *on behalf of* Mr. William J. Anderson

Yale University *on behalf of* Mr. Andrew T. Allan and Mr. Ely Kirschner

A different but related activity to the Foundation's efforts in education is the grant made to support the publication of a brochure for use in recruiting able individuals to the field of pharmacology. A grant of up to $22,000 has been made to the American Society of Pharmacology and Experimental Therapeutics (ASPET) for this purpose. Over the past several years, ASPET has distributed over 450,000 copies of a brochure entitled "A Career in Pharmacology," which was written to attract high school and beginning college students to the field of pharmacology. The grant will be used to update this brochure, which now is to be aimed at the more advanced student.

Pharmacologic-Pathology. A postdoctoral program offered by the Foundation is the "PMA Foundation Fellowship Awards in Pharmacologic-Pathology." The designation "pharmacologic-pathology" refers to the effects of drugs on morphologic structure in a very modern sense. Pharmacology has traditionally developed in the wake of advances in other sciences, particularly of biochemistry and physiology. Now, pharmacology, through this program, has an opportunity to follow in an entirely new direction as a result of modern anatomic studies that are reviewing the ultramicroscopic structure of cells.

Biochemists, cellular biologists, and modern structural researchers have joined hands to define, in many instances, the actual biochemical and functional role of particular cellular organelles. To further the interdisciplinary approach to common problems in the fields of structural studies and pharmacology, personnel skilled in both cellular biology and pharmacology will be needed. This fellowship program is designed to encourage good, young investigators from either pharmacology or the structural sciences to pursue training in the complementary field to enable them to attack important problems which lie in the middle ground. A yearly fund of $70,000 has been set aside for this program.

These fellowships are for two years each with the stipend level variable to keep within the existing stipend structure of the applicant university.

David W. Hiott, Ph.D.

Recipients of the first awards which began July 1, 1968, are:

- David W. Hiott, Ph.D., Department of Pharmacology, Medical College of South Carolina. Dr. Hiott will receive training in the procedures of autoradiography and in certain techniques and interpretations of histochemistry, particularly at the electron microscopic level. His program will proceed from his present base in which he has complete charge of an electron microscope facility and is engaged in an examination of ultrastructure changes produced by recognized cardiac drugs. He will give special attention to previously unrecognized drug changes in subcellular organelles as they may occur at the lower dose levels. The re-

John O. Lindower, M.D.

Timothy H. Mathew, M.D.

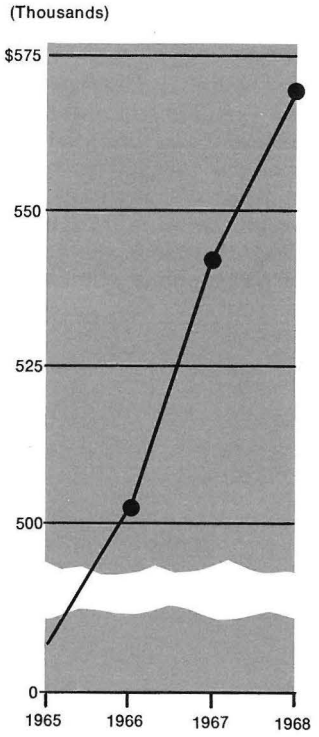
search efforts for the immediate future will be directed towards the investigation of ultrastructural changes in canine cardiac muscle by various dosage levels of digoxin.

• John O. Lindower, M.D., Department of Pharmacology, The Ohio State University. Dr. Lindower has completed all of his general requirements for his Ph.D. degree in Pharmacology and is presently engaged in full-time research for the Ph.D. Dr. Lindower will seek to establish the subcellular distribution of several radioactive digitalis glycosides and to determine the effect on muscle contraction and the toxic effects of these drugs. The subcellular fractionation methods presently used by Dr. Lindower will be augmented by electron microscopic fine-structure changes that occurred during digitalis perfusion of hearts as well as studies to localize radioactive glycosides by electron microscopic autoradiography.

• Timothy H. Mathew, M.D., Renal and Electrolyte Division, Georgetown University Hospital. His previous training and current interests have been oriented towards renal pharmacology from the vantage point of a clinical nephrologist. Dr. Mathew will continue his work in the Renal and Electrolyte Division. His work will center on the renal handling of various therapeutic agents and their associated pathological effects.

foundation finances

PMA Foundation
Contribution Income
1965-1968



Contributions are accepted from corporate and individual sources. The Foundation does not accept contributions which are so restricted as to place their use outside the policies of the Foundation. Contributions to the Foundation are also deductible for Federal income tax purposes.

The Board of Directors of the Foundation decided at the outset that, as a minimum, annual contributions of $500,000 would be sought for each of the first three years of the Foundation's existence, extending through 1968, with larger amounts anticipated thereafter. In requests for voluntary support to the PMA Member Firms, a guideline is suggested. Each firm is asked to consider a contribution equal to .015% of its domestic and international pharmaceutical sales.

Income. Total income in 1968 was $609,895. Of this amount, $567,951 came from contributions. The balance of $41,944 came from investments and a refund of an unexpended balance from a grant. The 1968 contributions represent an increase of approximately 5% over the $543,392 received in 1967 and about a 13% increase over the $503,297 received during 1965-1966.

Contributions were received from approximately three out of every four PMA Member Firms. Two out of every three PMA Associates also joined in supporting the Foundation. Contributions were received from a number of individuals and industry-related firms.

Expenditures. Grants, Foundation-sponsored programs and administrative expenditures for 1968 amounted to $505,492. Of this amount, $435,631 represent expenditures for grants and Foundation-sponsored programs. There was a fund balance of $725,571 as of December 31, 1968. This figure, however, does not reflect the tentatively authorized, undisbursed amounts for some of the grants and programs described earlier. The Foundation will report these amounts as expenditures when the funds are disbursed. As of December 31, 1968, this contingent liability totaled $1,024,367. Some of these grants represent amounts to be paid over the next three years. Part of this liability will be met from anticipated income in 1969 and succeeding years. During 1969 the estimated amount to be paid on this liability totals $540,000.

Financial Reports. The Foundation's financial position as of December 31, 1968, has been audited by the accounting firm of Ernst and Ernst. Copies of this statement will be supplied upon request.

Financial statements have been issued quarterly during 1968. These reports have been prepared by the Washington, D.C., accounting firm of Buchanan & Company. These cumulative quarterly reports will continue to be distributed in 1969.

STATEMENT OF INCOME AND EXPENDITURES

For the year ended December 31, 1968

Income

Contributions—Note a	$567,951
Income from investments	39,451
Refund of unexpended balance of prior year's grant	2,493
TOTAL INCOME	$609,895

Expenditures

Grants—Note b	
Georgetown—Kidney Fund	20,000
Regents of the University of California	20,000
University of Southern California School of Medicine	24,000
Institute of Experimental Pathology and Toxicology	25,000
Stanford Research Institute	17,964
National Academy of Sciences	10,000
University of Utah	18,000
Tufts University	13,720
Medical Student Traineeships in Clinical Pharmacology	20,000
Faculty Development Awards in Clinical Pharmacology	107,821
Fellowships in Pharmacologic-Pathology	34,500
Children's Hospital Research Foundation	75,000
University of Montreal	13,000
Universities Associated for Research and Education in Pathology, Inc. (Registry of Tissue Reactions to Drugs, AFIP)	27,226
Regents of the University of California (Kenneth L. Melmon, M.D.)	9,400
	$435,631
Administrative expenses	69,861
	$505,492
Excess of income over expenditures	104,403
Fund balance at January 1, 1968	621,168
Fund balance at December 31, 1968	$725,571

Note a—The Foundation received contributions of $104,051 prior to December 31, 1968, which the Foundation has considered applicable to 1969 and, therefore, are not recorded as income in 1968.

Note b—The Foundation has committed itself, subject to review, to make certain research grants. At December 31, 1968, the amounts still to be disbursed *with respect to these grants aggregated $1,024,367, of which approximately $540,000 is expected to be* disbursed *during the year 1969. No liability has been reflected for these amounts at December 31, 1968.*

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 properly directed 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 *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 most directly advancing the purposes of the Foundation.

Those areas *not* supported within the existing guidelines are:

(1) Support of research on specific drugs. This exclusion is not meant to preclude support of projects which, of necessity, use a number of drugs or a class 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. This kind of activity is the proper concern of individual firms or research agencies.

(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 better be served by channeling the Foundation's available resources into other areas.

(3) Requests for funds for travel.

(4) Requests for funds to cover entertainment costs.

As of 1968, a policy has been instituted which limits research support to no more than a two-year commitment, but allows the grantee to request an extension for a third year at the end of the first year's activity, with a report of the first year's activity.

beginnings

For those of you who, through this Annual Report, learn of the Pharmaceutical Manufacturers Association Foundation for the first time, a brief resumé of the history which led to its formation is in order. One event most influential in promoting the establishment of the PMA Foundation was the work and the Final Report of the Commission on Drug Safety, a study group formed by the Pharmaceutical Manufacturers Association in the Fall of 1962. The Commission was charged to make a study of the entire problem of drug safety and to come forth with recommendations. It carried out its work during the time of the urgency of the thalidomide situation. Special attention was given by the Commission initially to drug-induced fetal malformations. It became evident, however, that the most profitable line of inquiry would be to attack the overall problem of drug safety.

This Commission of distinguished membership, experts from universities, industry and government, arrived at a series of recommendations. A continuing theme expressed in a variety of ways by these authorities was that the pharmaceutical industry should show more interest in the conduct of basic studies in drug toxicology, with the suggestion that co-operative sponsorship of such fundamental projects would have the greatest potential for uncovering new information. To make such studies possible, the Commission suggested a number of alternative mechanisms.

One was to establish a foundation. This, as well as many of the Commission's other recommendations, was considered by the PMA Board of Directors for some months following publication of the Commission's report. On May 31, 1965, the PMA announced the establishment of the PMA Foundation. The initial operating funds were supplied by the PMA, and sustaining support for the Foundation has come from voluntary contributions of PMA Member Firms and Associates, industrial concerns, organizations and individuals with an interest in health care.

organization and administration

E. Gifford Upjohn, M.D.

C. Joseph Stetler

Raymond M. Rice, M.D.

Thomas E. Hanrahan

The PMA Foundation operates through a Board of Directors and three advisory committees. The Chairman of the Board is E. Gifford Upjohn, M.D., C. Joseph Stetler is President, Raymond M. Rice, M.D., is Vice President, and Thomas E. Hanrahan is Executive Director.

At the PMA Annual Meeting in 1968, Daniel C. Searle, President, G. D. Searle & Co., and Foster B. Whitlock, member, Executive Committee, Johnson & Johnson, were elected to the Board of Directors of the Foundation to fill the vacancies created by the resignations of William N. Creasy, then President of Burroughs Wellcome & Co. (U.S.A.) Inc., and Lyman C. Duncan, Vice President, American Cyanamid Company.

In continuing to seek the most worthwhile activities for support, the Board of Directors has had the advice of extremely knowledgeable individuals, serving on three advisory committees.

The Scientific Advisory Committee has the responsibility of making recommendations to the Board of Directors on all grant requests and on self-initiated undertakings. Irwin C. Winter, Ph.D., M.D., Vice President, Medical Affairs, G. D. Searle & Co., Chicago, Illinois, is Chairman of this committee. To increase its effectiveness, the Chairmen of the Medical and the Research and Development Sections of the PMA were invited to serve as ex-officio members of the Committee.

The Advisory Committee to the "Faculty Development Awards in Clinical Pharmacology" program is charged with making recommendations to the Board of Directors on all applications received for these awards, as well as those applications received under the "Medical Student Traineeships in Clinical Pharmacology" program. The Chairman of this committee is Thomas C. Chalmers, M.D., Assistant Chief Medical Director for Research and Education in Medicine, Veterans Administration, Washington, D.C.

The Advisory Committee to the "PMA Foundation Fellowship Awards in Pharmacologic-Pathology" program has the responsibility for making recommendations to the Board of Directors on all applications under this progrem. The Chairman of this committee is Walter F. Riker, Jr., M.D., Chairman, Department of Pharmacology, Cornell University Medical College, New York, New York.

Officers and Staff

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E. Leong Way, Ph.D.
Professor of Pharmacology
School of Medicine
University of California
San Francisco, California

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Assistant Chief Medical Director
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Veterans Administration
Washington, D.C.

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Vice President for Research
Hoffmann-LaRoche, Inc.
Nutley, New Jersey

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Director of Planning
Lederle Laboratories
Pearl River, New York

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Indiana University
Indianapolis, Indiana

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Associate Professor of Medicine
and Pharmacology
Vanderbilt University, School of
Medicine
Nashville, Tennessee

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

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Detroit, Michigan

Eugene A. Stead, Jr., M.D.
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Duke University Medical Center
Durham, North Carolina

***Irwin C. Winter, Ph.D., M.D.**
Vice President, Medical Affairs
G. D. Searle & Co.
Chicago, Illinois

** ex officio—as Chairman of Scientific Advisory Committee*

PMA FOUNDATION FELLOWSHIP AWARDS IN PHARMACOLOGIC-PATHOLOGY ADVISORY COMMITTEE

Walter F. Riker, Jr., M.D.

contributors

PMA Member Companies

Abbott Laboratories
Alcon Laboratories, Inc.
    Conal Pharmaceuticals, Inc.
Allergan Pharmaceuticals, Inc.
American Cyanamid Company
    Davis & Geck
    Fine Chemicals Department
    Lederle Laboratories Division
American Home Products Corporation
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Organon, Inc.
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(S. B. Penick Foundation)
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Philips Roxane Laboratories, Inc.
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(Warner-Lambert Pharmaceutical Co.)
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(W. M. Armistead Foundation)
William N. Creasy
Frank J. Corbett, Inc.
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Reader's Digest Foundation

applications

The Foundation welcomes requests for support and suggestions for projects from qualified institutions and individuals.

It is suggested that the requests for assistance take the form of a letter, outlining the subject, purposes, scope, principal researchers, curriculum vitae and bibliographies, budget and other sources of present or anticipated financing of the undertaking. Letters should be addressed to:

C. Joseph Stetler, *President*
Pharmaceutical Manufacturers Association Foundation, Inc.
1155 Fifteenth Street, N. W.
Washington, D. C. 20005

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