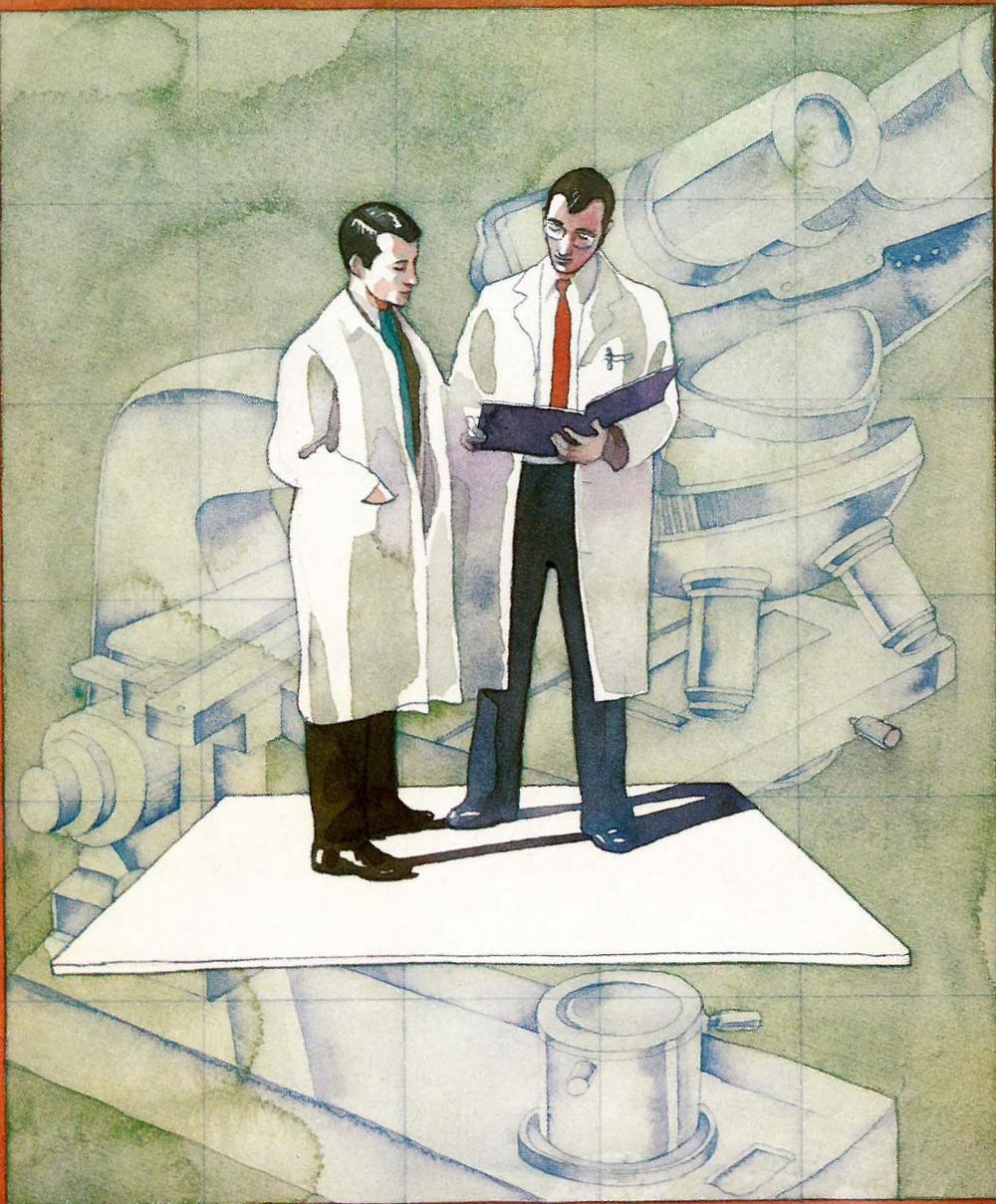


FROM PROJECTS TO PEOPLE



1971 Annual Report
Pharmaceutical Manufacturers
Association Foundation, Inc.



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FROM PROJECTS TO PEOPLE

Phase I—Phase II, household economic words in 1971. The end of one phase, the beginning of another with all their impact on wages, prices, inflation. We are familiar indeed with discussions of these governmental controls on the U.S. economy during 1971.

The PMA Foundation also experienced the end of one phase and the beginning of another during 1971. The changes in priorities, which have resulted were not sudden or dramatic. Rather, the Foundation's transition from one phase to another blended alternate programs into a smooth, continuous pattern.

The initial five-year program of the Foundation represents Phase I. From 1966 through 1970, support was characterized by relatively large research project grants. It was also during this time that the Foundation's programs of education and training support were first offered. In mid-1968 the expenditure of funds was about equally divided between research and educational support. By the end of 1970 educational programs received three of every five support dollars.

In 1971, the PMA Foundation Board of Directors took action which will result in a further increase in the level of educational support by establishing a goal for future support of 80% for education and 20% for research. With this action, Phase II of the Foundation's program development began, a phase to be marked by an expansion of current educational programs and, when feasible, the offering of programs already conceptualized, but awaiting funding.

This decision to give priority to education and training rather than research projects was not casually made. Research efforts supported by the Foundation have showed many positive results. However, it has become increasingly difficult to identify an effective role for the Foundation in providing small, partial research support.

In the drive to develop well-defined and feasible programs, the Foundation has continuously evaluated its efforts. Out of this examination, a belief developed that even greater benefits could be achieved with the funds entrusted to the Foundation by concentrating on educational support for talented scientists in the early stages of their careers. Thus, direct educational support moved to the fore as a more lasting way for the Foundation to contribute to the future of the biomedical sciences upon which health progress and the growth of the pharmaceutical industry vitally depend. Research support will continue to be available but primarily in ways different from those of the initial years. One such new avenue is the Research Starter Grants program described later in this report.

The first five years of Foundation program development have been characterized as "building for tomorrow". That "tomorrow" began in 1971. To continue its effectiveness, the Foundation will look to its contributors for additional resources. As tangible measures of accomplishments become evident, the Foundation is confident that increased support will follow.

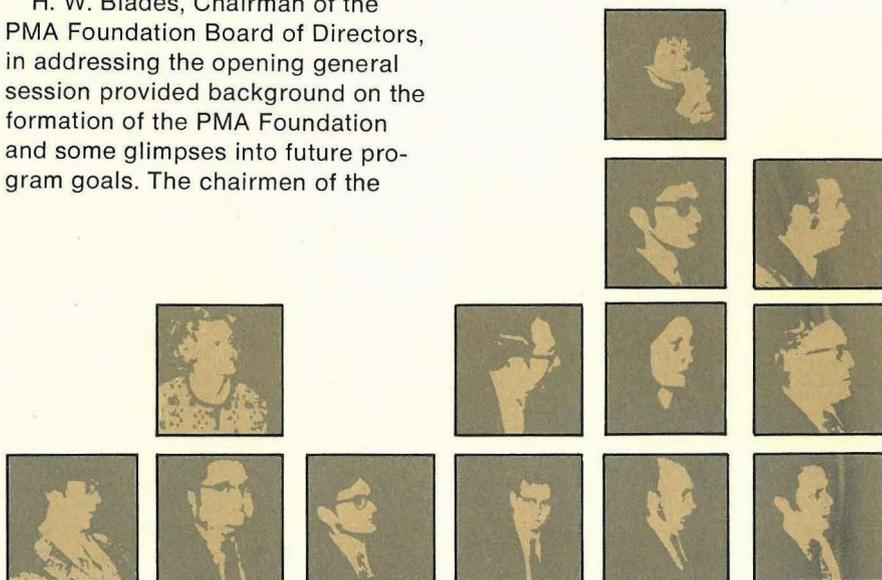
INFORMATION EXCHANGE

The recipients of awards under the PMA Foundation two postdoctoral education programs and members of the Foundation's three advisory committees spent a productive day and a half sharing experiences, concerns, and aspirations at a meeting held December 13-14, 1971 in New York City. This conference provided the opportunity for a direct assessment of the Foundation's programs. It also enabled awardees to exchange information on their current research and teaching responsibilities. The only other meeting of this kind was held in 1969. Since that time, the number of scientists supported under each of the postdoctoral programs—the faculty awards in clinical pharmacology and the fellowship program in pharmacology-morphology—has doubled.

H. W. Blades, Chairman of the PMA Foundation Board of Directors, in addressing the opening general session provided background on the formation of the PMA Foundation and some glimpses into future program goals. The chairmen of the

three advisory committees then described the program areas for which their committees have responsibility.

The meeting next divided into two groups. The clinical pharmacologists, in a discussion group under the chairmanship of Dr. John Oates, Professor of Medicine and Pharmacology, Vanderbilt University, heard presentations on some of the major areas of research engaged in by five of their group. The group also engaged in a wide-ranging discussion of curriculum needs, teaching methods and communication with house staff and the practicing physician.



In the workshop jointly moderated by Dr. Walter Riker, Jr., Professor and Chairman, Department of Pharmacology, Cornell University Medical College and Dr. Don Fawcett, Hersey Professor of Anatomy, Harvard Medical School, the pharmacology-morphology fellows explored the range of their research interests, including teratologic concerns in drug testing, the use of fine-structure techniques to localize the cellular actions of drugs, and pharmacology-morphology in the study of function and drug action in the nervous system.

An added dimension of value to the discussions of both groups of awardees resulted from the presence of the members of the Foundation's advisory committees, all recognized leaders in fields covered by the postdoctoral programs.

A joint session between those attending the Foundation meeting and the Board of Directors of the Pharmaceutical Manufacturers Association was also held. In his welcoming remarks, Mr. Henry Gadsden, Chairman, PMA Board of Directors commended the many excellent reports on the progress of the Foundation from the chairmen of the advisory committees. He indicated that while much of the enthusiasm that these chairmen have for the Foundation is transmitted in these reports, nothing can replace the direct experience of meeting those about whom the reports have been made. As for the awardees, they emphasized that the opportunity to exchange views with the leadership of the pharmaceutical industry was particularly stimulating.



ACTIVITIES

Since its formation, approximately \$3,400,000 has been authorized by the PMA Foundation for a variety of workshops, conferences, research projects and educational programs. Of this amount \$1.4 million has gone to support research and about \$1.6 million to educational awards. The remaining \$400,000 has been used largely for meetings, with a smaller portion for publications.

WORKSHOPS AND CONFERENCES

Since assistance for the first workshop in drug metabolism was authorized by the Foundation in late 1965, particularly pertinent meetings have continued to receive financial aid.

Clinical Pharmacology. *An award of up to \$176,880 was made to support a four-year effort by the American Society of Pharmacology and Experimental Therapeutics directed at advanced pharmacology students.*

The funds support four to six week courses for Ph. D. candidates at selected universities where highly specialized studies are offered.

Through this award, training in pharmacology for these selected doctorate candidates is enhanced in departments which are very capable in certain subject areas. Up to 50 doctoral candidates can be accommodated each year. The American Foundation for Pharmaceutical Education also has provided financial support for this activity.

The first host was the University of Minnesota, Department of Pharmacology, and the director was Gilbert J. Mannering, Ph. D., Professor of Pharmacology. This four week session held in 1969 dealt with drug metabolism and biochemical pharmacology.

The second location was the College of Physicians and Surgeons, Columbia University, New York City for four weeks beginning July 6, 1970. The director was Brian F. Hoffman, M.D., Chairman, Department of Pharmacology. The area of instruction was cardiovascular pharmacology.

The third location was the University of California, San Francisco Medical Center, for four weeks beginning July 6, 1971. The director of the session was Robert M. Featherstone, Chairman, Department of Pharmacology. The area of instruction was molecular pharmacology.

The last of the sessions will be hosted in 1972 by Vanderbilt University, Department of Pharmacology. The course will deal with neuropsychopharmacology concerns.

Bioavailability. *A grant of \$7,500 was made to the National Academy of Sciences-National Research Council for support of the Conference on Bioavailability of Drugs held November 22-23, 1971 in Washington, D.C.* The conference, attended by over 600 individuals, was sponsored by the Food and Drug Administration, National Formulary, Academy of Pharmaceutical Sciences—American Pharmaceutical Association, National Academy of Sciences and the PMA Foundation.

The purpose of the conference was to assess the current status of information on bioavailability and recommend further research. The papers presented at the Conference are to be published and should be available by mid-1972.

Immunopharmacology. *A grant of \$20,350 was made to the National Academy of Sciences for support of a Workshop on Immunopharmacology held at New York University, November 15-19, 1971, under the direction of Bert La Du, M.D., Ph. D., Chairman, Department of Pharmacology at the University.* This workshop, attended by approximately 40

participants, was aimed at pharmacologists not totally familiar with the principles and applications of immunology. The format of the meeting was structured to introduce immunopharmacology and those immunological principles applicable to pharmacological research problems.

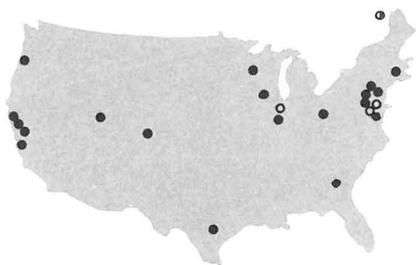
Presentations made at this workshop are to be published by mid-1972.



Participants in a discussion group at the Workshop on Immunopharmacology held at New York University, November 15-19, 1971.

Mutagenicity. A grant of \$10,000 was made for support of an *invitational Workshop on Mutagenicity held at Roger Williams General Hospital, Providence, Rhode Island, July 26-28, 1971, under the chairmanship of Paul Calabresi, M.D., Physician-in-Chief, Roger Williams General Hospital.* The workshop grew out of a recommendation from a Conference on Evaluating Mutagenicity of Drugs and Other Chemical Agents, held in November, 1970 and attended by hundreds of scientists, that a smaller workshop type meeting should be convened.

The purpose of the workshop was to demonstrate the various current tests for mutagenesis in a laboratory setting using pre-prepared experiments. The workshop was designed for those in academic, government and industry administrative research policy positions rather than for scientists working directly in the laboratory on mutagenicity testing.



Geographical distribution of Foundation general research grants, 1966-1971.

- One
- More than one
- ⊙ Outside U.S.

RESEARCH GRANTS

An important Foundation activity is support of fundamental research in drug toxicology. Since 1966 a total of 26 general research grants have been made for this purpose. Support on nine of these has terminated. The remaining 17 grants continue over various periods of time through 1973.

In 1971 new grants were made to the Medical College of Georgia; the University of Illinois, Urbana; and Universities Associated for Research and Education in Pathology, Washington, D.C.

Fourteen grants current in 1970 continued into 1971. These are:

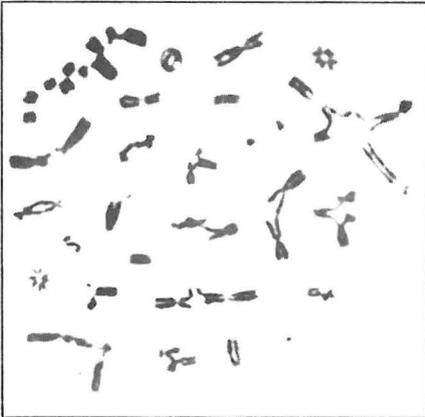
- Rutgers University, College of Pharmacy, Newark, New Jersey
- Georgetown University School of Medicine-School of Dentistry, Department of Pharmacology, Washington, D.C.
- Georgetown University, Renal and Electrolyte Division, Washington, D.C.

- Albany Medical College of Union University, Institute of Experimental Pathology and Toxicology, Albany, New York
- Children's Hospital Research Foundation, Institute for Developmental Research, Cincinnati, Ohio
- University of Chicago, Department of Obstetrics and Gynecology, Chicago, Illinois
- University of Illinois at the Medical Center in Chicago, Department of Pediatrics
- University of Minnesota School of Medicine, Department of Pharmacology, Minneapolis, Minnesota
- Rochester University School of Medicine, Department of Pharmacology and Toxicology, Rochester, New York
- University of Oregon Dental School, Department of Biochemistry, Portland, Oregon
- Hahnemann College of Medicine, Department of Anesthesiology, Philadelphia, Pennsylvania
- State University of New York in Buffalo, Department of Pediatrics
- The University of Texas Medical Center in Dallas, Department of Pediatrics
- Stanford University Medical Center, Department of Pediatrics, Stanford, California

In addition, a program of *Research Starter Grants* was offered for the first time in 1971. These grants are described at the end of this section of the report.

The 17 current general research grants fall into the following categories:

Animal-Human Predictability Studies. A grant of \$78,654 over a two-year period beginning January 20, 1969, to the Department of Obstetrics and Gynecology, Chicago Lying-In Hospital, Pritzker School of Medicine, University of Chicago, concluded in 1971. The principal investigator was Anthony P. Amarose, Ph. D., Associate Professor, Department of Obstetrics and Gynecology, and the co-investigator was Charles R. Schuster, Ph. D., Associate Professor, Departments of Psychiatry and Pharmacology.



The combined chromosomes form a composite cell of the rabbit animal model being studied by Dr. Anthony Amarose, University of Chicago. Most of the known types of chromosome damage are depicted in this cell. Development of the animal model was dependent on obtaining chromosome damage in the circulating lymphocytes of the experimental animal using a pharmacologic agent known to cause the same types of damage in human cells. Magnification x 2052

This work was aimed at determining whether a relationship exists between chromosome damage and drug intake. The study measured the response in the chromosomes of lymphocytes (a form of the white blood cell) and bone marrow cells to drug stimuli.

A full report on the study was published in the *Archives of General Psychiatry*, August, 1971, entitled "Chromosomal Analyses of Bone Marrow and Peripheral Blood in Subjects with a History of Illicit Drug Use."

A grant of \$15,000 for one year beginning July 1, 1971, was made to Henry L. Price, M.D., Professor of Anesthesiology, Hahnemann College, to support research into the state of circulatory depression which attends the administration of most anesthetics. Specifically, it has been found that certain anesthetics cause an activation of receptors in the heart itself which are capable of restoring circulatory function to or toward normal as anesthesia progresses,

The research will attempt to discover an animal model suitable for the study of this phenomenon of "recovery" from or "tolerance" to an anesthetic while it is still being given. By use of the animal model, it is then proposed to learn the mode of action involved whereby anesthetics can act to produce antagonism to their own depressant actions on the heart. Studies will also be carried out in man.



Dr. Edward Voss, University of Illinois, studying photomicrographs of antibody producing cells as part of ongoing immunological studies.

A grant of \$8,000 over a two year period beginning March 1, 1971 was made to Edward W. Voss, Jr., Associate Professor, Department of Microbiology, University of Illinois to allow the continuation of immunochemical studies with lysergic acid (LSA) and lysergic acid diethylamide (LSD). The approach has been to use LSA as a haptenic determinant group. Preliminary studies of the conjugation of LSA to carrier proteins suggest that the conjugation involves the E-aimo groups of lysine.

Serum samples from mice and rabbits immunized with the LSA-protein conjugates preliminarily indicated that the sera contain antibodies specific for the LSA determinant group. Therefore, among the current objectives of the study are to elect antibodies specific to the LSA haptenic group and to determine if these antisera neutralize the biological effects of hallucinogenic drugs.

Clinical Pharmacology. *A grant of \$51,850 for two years beginning July 1, 1970, made to William T. Beaver, M.D., Associate Professor of Pharmacology, Department of Pharmacology, Georgetown University School of Medicine and Dentistry, to establish a facility for studying the comparative effects of drugs on subjective responses entered its final year in 1971.*



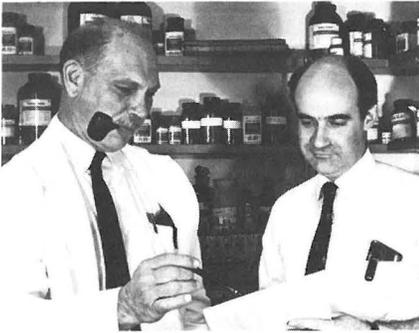
Nurse-observer obtaining permission from patient's physician for participation in the study at Georgetown University of the comparative effects of drugs on subjective responses.

The investigation primarily is concerned with the evaluation in patients of drugs whose major effect is in the treatment of symptoms such as pain, anxiety, insomnia and nausea. The initial studies are directed towards the evaluation of potent analgesics in patients with postoperative pain.

An initial standardization study comparing the analgesic efficacy of a morphine standard with a morphine test drug in postoperative patients from the orthopedic, gynecologic and general surgical services has been completed. The study established the value of using the incomplete block, sequential decision making approach to analgesic studies in these kinds of patients.

A grant of \$15,000 for one year beginning July 1, 1970, made to Louis Lasagna, M.D., Professor of Pharmacology, University of Rochester School of Medicine, for research into gastric physiology and metabolism in affecting the fate of a series of compounds concluded in 1971. The long-prevalent notion that the stomach acts primarily as a barrier to passive diffusion of drugs into the circulation was studied. The study examined a series of compounds in both animals and man, with attention paid to such factors as metabolism by the gastric mucosa, gastric emptying, gastric pH, etc., and ways in which these factors influenced the therapeutic and toxic effects of drugs in man.

A grant of \$17,042 for one year beginning June 1, 1970, made to Donald B. Hunninghake, M.D., Assistant Professor of Medicine and Pharmacology, Department of Pharmacology, University of Minnesota Medical School, to support a project primarily designed to evaluate the utility of plasma drug levels as a guide to more effective therapy concluded in 1971. In this study, individual titration of dose and dosage schedules for patients was done on the basis of plasma level of drugs concentrating initially on the anticonvulsant drugs. The effects of this individual titration on both efficacy and toxicity were evaluated. A number of papers are anticipated from this study. Two will be published in 1972, one in *Clinical Pharmacology and Therapeutics*, and the other an abstract for the Academy of Pharmaceutical Sciences, American Pharmaceutical Association.



Dr. William van B. Robertson (left) and Dr. John Miller, Stanford University, reviewing data from study of drugs and the lupus syndrome.

A grant of \$30,000 over a two-year period which began March 1, 1971, was made to John J. Miller, III, M.D., Ph. D., Assistant Professor of Pediatrics, Department of Pediatrics, Stanford University School of Medicine for a study of the relation of drugs to the lupus syndrome. The purpose of the research is to define the way in which certain drugs induce formation of anti-nuclear factors, a group of abnormal antibodies, and to define the relation between these drugs and the spontaneously occurring disease, systemic lupus erythematosas.

The specific purpose of the work is to discover which drugs are most likely to cause anti-nuclear factors to appear in children and to determine how many children develop antinuclear factors and the associated disease.

Two approaches have been used, one clinical and one biophysical. The research group has been studying children who develop the abnormal antibodies while receiving anticonvulsants. A statistically significant increase in the incidence of anti-nuclear antibodies has been observed in girls receiving these drugs, but not in the boys.

The biophysical studies have primarily been concerned with a search for binding of lupus-inducing drugs to DNA, since antibodies to DNA are considered important in the pathogenesis of lupus.

Dialyzable Drugs. *A grant of \$20,000 a year for five years for a total of \$100,000 beginning January 1, 1967, to the Renal and Electrolyte Division, Georgetown University Hospital, concluded in 1971. George E. Schreiner, M.D., Professor of Medicine and Director, Renal and Electrolyte Division, was the principal investigator. These funds were provided to support research related to the hemodialysis of drugs and poisons and to produce an annual registry of dialyzable drugs 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 the diffusion through a semi-permeable membrane.*

In 1971, the research group prepared and published, as it had the prior four years, a review of dialyzable drugs and poisons. This appeared in the 1971 TRANSACTIONS of the American Society of Artificial Internal Organs.

The grant has also enabled the Renal and Electrolyte Division to maintain the capability of studying new drug-overdose cases as they arrive on the clinical service. Data obtained in this way is obtainable through no other form since it is not permissible to give drugs in such a level in human research.

Drug Metabolism. *A grant of \$30,000 over a two-year period beginning November 1, 1971 was made to Edward Bresnick, Ph. D., Chairman, Department of Cell and Molecular Biology, Medical College of Georgia for study of the mechanisms by which the mixed-function oxidase system is regulated during liver development.* A second aspect of the study will deal with research aimed at understanding the mechanisms by which environmental factors such as polycyclic hydrocarbons are able to induce the drug metabolizing enzyme system.

These two aspects are related in that they provide the basis for an exhaustive study of the mechanisms by which developmental and environmental influences affect the activity of the mixed-function oxidase system.

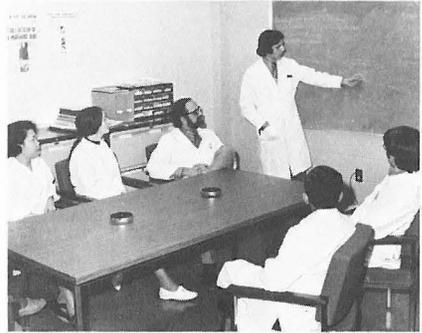
Drug-Related Structural Studies.

A grant of \$25,000 a year for a four-year period which began August 1, 1967, totaling \$100,000 to the Institute of Experimental Pathology and Toxicology of the Albany Medical College of Union University, Albany, New York concluded in 1971. The principal investigator was Frederick Coulston, Ph. D., Director of the Institute. Funds during the four years accelerated the Institute's studies of the relation of structural changes in the subcellular organelles of important tissues to the actions of chemicals and drugs. This program had as its purpose the establishment of selected critical areas of experimentation in animals with the anticipation that valid prediction of safety can be made in man with limited, but precise investigation.

Drug Surveillance. *A grant of \$25,000 was made to the Universities Associated for Research and Education in Pathology for support during 1971-1972 of the Registry of Tissue Reactions to Drugs, Armed Forces Institute of Pathology. The Registry is co-sponsored and supported by the American Medical Association, the Food and Drug Administration and the PMA Foundation. Nelson S. Irey, M.D., is the Registrar.*

The Registry obtains biopsy and autopsy tissue specimens on a voluntary reporting basis from participating pathologists, from industry and the government. The Registry subjects the specimens to microscopic examination and reports its findings to the referring pathologist.

A set of educational publications which have been produced by the Registry entitled "Diagnostic Problems and Methods in Drug-Induced Diseases", is available to medical schools, along with a set of lantern slides.



Dr. Ernest Zimmerman (standing) and staff of the Division of Fetal Pharmacology, Institute for Developmental Research, discussing next steps in the protocols of ongoing research in the Division.

Fetal and Neonatal Pharmacology.

A grant of \$50,000 a year for five years for a total of \$250,000 made in 1967 to Josef Warkany, M.D., Professor of Research Pediatrics, on behalf of the Children's Hospital Research Foundation for partial support of the activities of the Division of Fetal Pharmacology of the Institute of Developmental Research entered its last year in 1971. The Institute, which opened June 1968, has used Foundation support primarily in the Division of Fetal Pharmacology to support staff and purchase the equipment needed for the basic research within this unit. Ernest F. Zimmerman, Ph. D. is the Director of the Division.

The Division of Fetal Pharmacology has continued its interests in the area of drug-induced malformations. Research on glucocorticoid-induced cleft palate has recently been focused on the latent period—the time between the administration of the teratogen and the morphologic appearance of the malformation. Attention is also being paid to the mechanism by which the elevation of palate shelf has been slowed by the teratogen.

Investigations are also progressing in other divisions of the Institute being assisted by the Foundation's funds. Mechanisms of drug actions on embryos and fetuses are studies in the Division of Pathologic Embryology. The Division of Teratology and Genetics is involved in studies which have a special emphasis on congenital malformations of the central nervous system.



Dr. Charles Mize, right, and Dr. Howard Worthen, University of Texas, analyzing results from the biochemical and electron microscopic studies of toxic mechanisms of selected antibiotics.

A grant of \$30,000 over a two-year period which began February, 1971 was made to Charles E. Mize, M.D., Ph. D., Assistant Professor of Pediatrics, The University of

Texas Southwestern Medical School at Dallas for a study of selective antibiotic action on mammalian membrane assembly. The co-investigator is Howard G. Worthen, M.D., Ph.D., Professor of Pediatrics. The study is concentrating on the effects of certain antibiotics on selected new membrane formation essential to cell growth in renal tissue of rabbits. The response to various selected antibiotics is being investigated with radioactive tracer experiments, electron microscopic determination of anatomic changes and the enzymatic and chemical studies of the membranes.

A grant of \$17,150 for fifteen months beginning May 15, 1970, made to Walter L. Gabler, D.D.S., Ph.D., Associate Professor, Division of Oral Biology and Department of Biochemistry, University of Oregon Dental School, to study drug metabolism during pregnancy concluded in 1971. To examine the problem, an antiepileptic drug was tested on pregnant and non-pregnant Rhesus monkeys to determine if pregnancy alters the normal metabolism of an anticonvulsant drug. A reduction in metabolism of drugs during pregnancy can have significant pharmacological implications for both the mother and fetus, particularly if the drug is capable of interfering with protein synthesis.

One finding indicated that the retention time of the parent drug was prolonged in the pregnant monkey. Both plasma disappearance and urinary excretion of the drug was slower in the pregnant as compared to the non-pregnant monkey.

A grant of \$58,000 over a two-year period beginning May 1, 1970, made to Richard E. Behrman, M.D., then Professor of Pediatrics, Department of Pediatrics, University of Illinois at the Medical Center (Chicago) entered its second year in 1971. The study aims to characterize the pharmacologic effect of phenobarbital on fetal and newborn monkeys by evaluating the effects on blood pressure, heart rate, ECG, cardiac output, oxygen consumption and organ blood flows. Dr. Behrman accepted the Chairmanship of the Department of Pediatrics at the College of Physicians and Surgeons in late 1971, but remains a consultant to the study.

The kinetics of the placental transfer are being studied as well as the effects on the fetal and placental circulations, particularly the liver and brain. The investigations are attempting to compare the dose response relationships of the effects of phenobarbital on increasing bilirubin conjugating activity and on protecting the brain from asphyxia before and after birth to the dose response relationships for including fetal and newborn depression and hypotension. The observations are significant in increasing the understanding and the ability to evaluate the *in utero* and neonatal treatment of human infants with phenobarbital.

During the first year, studies in fetal baboons have been completed and have indicated, among other findings, that during steady state conditions phenobarbital is transferred across the placenta and this transfer is flow limited. The distribution of phenobarbital in the fetal tissues was characterized as well as the distribution of blood flow to each organ of the fetus.



An infant monkey involved in the University of Illinois study of the effects of drugs on the fetus. Here, the monkey is part of a study of regional circulation measurements.

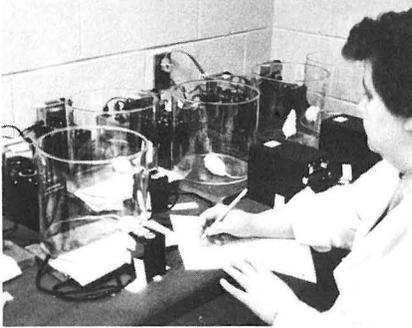
Nutritional Deficiencies—Drug

Action. A grant of \$29,459 over a two-year period beginning March 1, 1970 to Christina Vander-Wende, Ph. D., Professor of Biochemistry and Pharmacology, Rutgers University, entered its final year in 1971. The funds provide support for studies of the interaction of vitamin deficiencies and drug action. The extension of these studies will eventually include studies of protein deficiencies and a generalized malnutrition state on drug action and drug toxicity.

Initial studies have shown that older rats on thiamine-deficient diets were much more sensitive to the depressant effects of barbiturates than younger rats. The investigators have also found that with d-amphetamine, the deficiency state influences the toxicity of the drug differently depending upon whether the animals are isolated or whether they experience group interactions. Thiamine-deficient animals are protected significantly from the excessive toxicity in grouped situations.

Studies have been started on the effects of riboflavin deficiency on

drug actions. The biochemical studies required for understanding the course of development of this deficiency state have been completed and the drug studies begun. The riboflavin deficiency has proved to be more difficult to produce than the thiamine deficiency. In contrast to what was found in thiamine deficiency, the toxicity of amphetamine does not significantly change even in the grouped situation.



Dr. Christina VanderWende, Rutgers University, testing the effect of riboflavin deficiency in rats on the psychomotor activity induced by drugs.

A grant of \$44,590 over a two-year period, which began April 15, 1971, was made to Sumner A. Yaffe, M.D., Professor of Pediatrics, Department of Pediatrics, State University of New York at Buffalo, to study the effect that malnutrition may have on the activity of hepatic drug-metabolizing enzymes. Both acute and long-term effects of nutritional deficiency are being studied.

Initial studies with malnourished rats have involved different representative drugs for mixed-function oxidation reaction; nitro group reduction reaction; azo group reduction; and as substrates for glucuronide and sulfate conjugation. *In*

vitro measurements of drug metabolism were made at two ages: 21 and 50 days in both control and malnourished rats. Significant increases in specific activity were noted *in vitro*. To determine whether these drug metabolism changes affected drug action, hexobarbital was used in correlative *in vivo* studies. Preliminary studies show that sleep, the major action of hexobarbital, was longer in malnourished animals (160 ± 9 minutes) than in the controls (112 ± 6 minutes). Further studies of this difference are underway.

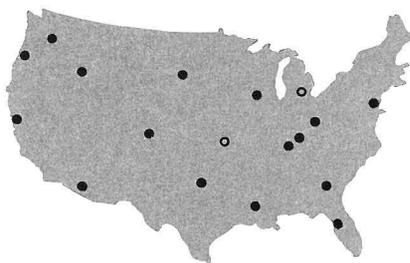
Research Starter Grants. *A program of Research Starter Grants was offered for the first time in 1971. These grants are intended to provide financial support for beginning investigators. The program offers a sum of \$5,000 a year for two years, with the second year contingent upon a continuing need for the funds. The research areas of interest within this program are in the fields of pharmacology, clinical pharmacology, and drug toxicology. The program has a budget of \$200,000 a year, allowing for up to 20 new research grants each year.*

In developing this program, the Foundation was motivated by the belief that a very real need exists among beginning investigators for "starter" funds, funds which could be used to generate data to serve as the basis to obtain greater amounts of support. The experience from the initial offering of the program, with over 150 applications, has proved this to be the case.

The first 20 research starter grants, beginning January 1, 1972 went to schools of pharmacy, schools of medicine and veterinary schools in all parts of the United States. The schools and the recipients of the research starter grants for 1972 are:

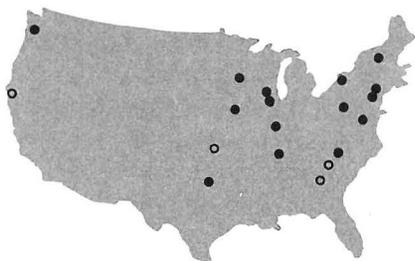
- Frederic C. Beuthin, Ph. D., College of Pharmacy, Idaho State University
- George M. Brenner, Ph. D., School of Pharmacy, South Dakota State University
- Yun-Lai Chan, Ph. D., Department of Pharmacology, School of Medicine, University of Louisville
- Claudia Crow, Ph. D., Department of Anatomy, Emory University, Woodruff Medical Center
- Thomas J. Fitzgerald, Ph. D., Department of Pharmacology, University of Kansas Medical Center
- Jay I. Goodman, Ph. D., Department of Pharmacology, College of Osteopathic Medicine, Michigan State University
- Susan Horwitz, Ph. D., Department of Pharmacology, Albert Einstein College of Medicine
- Phillip C. Jobe, Ph. D., and Gary G. Ferguson, Ph. D., School of Pharmacy, Northeast Louisiana University
- Ralph Kauffman, M.D., Department of Pediatrics, University of Kansas Medical Center
- William R. Kem, Ph. D., Department of Pharmacology and Therapeutics, College of Medicine, University of Florida
- Horace Loh, Ph. D., Department of Pharmacology, School of Medicine, University of California, San Francisco Medical Center

- Ralph E. Miller, M.D., D.Sc., Department of Pharmacology, University of Kentucky Medical Center
- George D. Olsen, M.D., Department of Pharmacology, University of Oregon Medical School
- Casey P. Robinson, Ph. D., College of Pharmacy, University of Oklahoma
- Charles F. Ryan, Jr., Ph. D., School of Pharmacy, University of Wisconsin
- Robert C. Schnell, College of Pharmacy, Washington State University
- Paul M. Stephen, M.D., Ph. D., and John O. Lindower, M.D., Ph. D., Department of Pharmacology, Ohio State University College of Medicine
- Paul D. Thut, Ph. D., Department of Pharmacology, College of Medicine, University of Arizona
- W. David Watkins, Ph.D., Department of Pharmacology, Medical Center, University of Colorado
- Frank Welsch, D.V.M., Department of Pharmacology, Michigan State University, College of Veterinary Medicine



Geographical distribution of Foundation awards under the "Research Starter Grants" program, 1971. (Grants beginning January 1, 1972)

- One
- More than one



Geographical distribution of Foundation awards under its "Faculty Development Awards in Clinical Pharmacology" program, 1967-1971.

- One
- More than one

EDUCATION AND TRAINING PROGRAMS

To further its objectives in the field of education, the Foundation sponsors two programs in clinical pharmacology and one in the combined fields of pharmacology and morphology.

The two clinical pharmacology programs have provided educational opportunities for a number of individuals at both the student and the faculty level.

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.* The level of support is variable but in keeping within the existing salary structure of the applicant university. The Board of Directors has established a fund of \$150,000 to finance the yearly awards.

With the awards scheduled to begin July 1, 1972, a total of 24 individuals have now been supported under this program since its inception in 1967. While the award is for a two-year period, a third year of support is available to those awardees who, at the end of their first year, show sufficient need for the third year. An additional fund of \$75,000 has been authorized to provide for the contingency of requests for a third year of support.

Recipients of new faculty awards, which begin July 1, 1972 are:

- David S. Alberts, M.D., Clinical Cancer Trainee, School of Medicine, University of California, San Francisco. Dr. Alberts will investigate, in humans, the correlation of drug concentration, distribution, route and method of administration of cancer chemotherapeutic agents with their effectiveness in tumor cell kill. He will make rounds with members of the clinical pharmacology unit and will be involved in weekly clinical pharmacology research seminars.
- Carlos A. Dujovne, M.D., Assistant Professor of Medicine, University of Kansas Medical Center. Dr. Dujovne will continue the clinical evaluation of drugs, especially hypolipidemic agents and evaluate hepatotoxicity through a variety of methods. He will participate in all of the faculty functions of the Pharmacology Department as well as in the conferences, seminars and trainee supervision of the Section on Clinical Pharmacology.



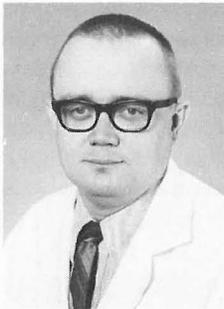
David S. Alberts, M.D.



Carlos A. Dujovne, M.D.



John S. Kaufmann, M.D., Ph. D.



Robert A. Mueller, M.D., Ph. D.



August Watanabe, M.D.

□ John S. Kaufmann, M.D., Ph. D., Assistant Professor of Medicine and Pharmacology, The Bowman Gray School of Medicine, Wake Forest. Dr. Kaufmann will evaluate drugs used in the treatment of high blood pressure, malignant diseases and those which effect blood cells and coagulation. He will continue his teaching responsibilities with the medical and graduate schools and plans to expand the school's clinical pharmacology teaching program for residents and interns.

□ Robert A. Mueller, M.D., Ph.D., Associate Professor of Anesthesiology, School of Medicine, University of North Carolina. Dr. Mueller will investigate cardiovascular and respiratory effects of Δ -9 tetrahydrocannabinol, a marijuana component,

and examine both sympathetic nervous system activity and the administration of anesthetics to hypertensive patients. He will continue his pharmacology courses for pharmacy, dental and medical students and other courses in clinical pharmacology of anesthetic agents.

□ August Watanabe, M.D., Assistant Professor of Medicine and Pharmacology, Indiana University. Dr. Watanabe will conduct research on the effects of certain drugs on myocardia metabolism. His teaching responsibilities will include clinical rounds with the house staff and lectures on therapeutics to medical students.

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

- Faruk S. Abuzzahab, Sr., M.D., Ph. D., Assistant Professor of Psychiatry and Pharmacology, University of Minnesota, is conducting research in both basic and clinical pharmacology.
- John S. Holcenberg, M.D., Associate Professor of Medicine and Pharmacology, University of Washington, Seattle, is extending his training in biochemical approaches to clinical pharmacology.
- John L. McNay, M.D., Assistant Professor of Pharmacology and Professor of Medicine, Emory University School of Medicine, is conducting research in renal physiology and pharmacology.

Recipients of awards which began July 1, 1968, and which were extended until June 30, 1971, are:

- William Y. W. Au, M.D., Associate 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., an Assistant Professor, Pharmacology and Medicine, Cornell University, when the award was made, has research interests in the cardiovascular field. He is presently Assistant Dean, Cornell University Medical College.
- Donald S. Robinson, M.D., Associate Professor of Medicine and Pharmacology and Director, Clinical Pharmacology Unit, University of Vermont, is involved in studies in biochemical pharmacology.

Recipients of awards which began July 1, 1969, are:

- Vincent S. Aoki, M.D., an Assistant Professor, University of Iowa, when the award was made, was involved in studies of the effects of drugs on the pulmonary vascular bed. He resigned a third year of support in December, 1971 to enter the private practice of medicine in Hawaii.
- Lester F. Soyka, M.D., Associate Professor of Pharmacology and Pediatrics, University of Illinois Medical Center in Chicago, is involved in research dealing with immaturity at the biochemical level and other developmental studies.
- Pate D. Thompson, M.D., an Instructor, University of California, San Francisco Medical Center, when the award was made, resigned the second year of the award to take a position of chief of a cardiac unit in a California hospital.
- Stanley C. Ushinski, M.D., an Assistant Professor of Pediatrics and Pharmacology, University of Pittsburgh, when the award was made, resigned the second year of the award to enter private practice.

Recipients of the awards which began July 1, 1970, are:

Arthur J. Atkinson, M.D., Assistant Professor of Medicine and Pharmacology, Northwestern University Medical School, is conducting research into cardiac drugs in relation to their effectiveness.

Samuel A. Cucinell, M.D., an Assistant Professor of Medicine, Emory University School of Medicine, when the award was made, was involved in drug metabolism research in man. He resigned the second year of the award to assume the responsibility as Chief, Clinical Medicine, U.S. Army Edgewood Arsenal.

Aryeh Hurwitz, M.D., Assistant Professor of Medicine and Pharmacology, Clinical Pharmacology-Toxicology Center, University of Kansas Medical Center, is conducting research into the mechanism of action of compounds which are poisonous to liver cells.

Recipients of the awards which began July 1, 1971, are:

I. David Goldman, M.D., Assistant Professor of Medicine and Pharmacology, University of North Carolina School of Medicine. Dr. Goldman is studying the mechanisms which facilitate drug-cell interactions.

Urs A. Meyer, M.D., Instructor of Medicine, University of California, San Francisco Medical Center. Dr. Meyer's primary research interest is in the area of drug metabolism, with the goal of developing an *in vitro* model of drug-induced increase in synthesis of P-450 enzymes using cell culture techniques.

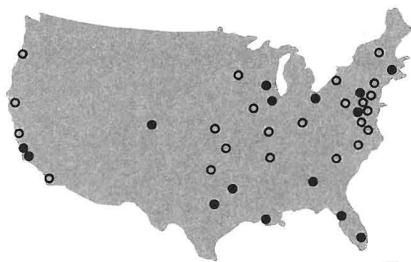
Alan S. Nies, M.D., Assistant Professor of Medicine and Pharmacology, Vanderbilt University, School of Medicine. Dr. Nies is studying the effects of alterations of regional blood flow by disease or drugs.

Harold C. Strauss, M.D., Associate in Pharmacology, College of Physicians and Surgeons, Columbia University. Dr. Strauss is engaged in studies designed to improve understanding of antiarrhythmic drug actions.

Wilmer Leigh Thompson, M.D., Ph. D., Assistant Professor of Medicine and Assistant Professor of Pharmacology and Experimental Therapeutics, Johns Hopkins University. The award has enabled Dr. Thompson to continue his research on drug therapy in seriously-ill patients.

Thomas L. Whitsett, M.D., Assistant Professor of Medicine and Pharmacology and Acting Associate Director of the Clinical Pharmacology Division of the University of Oklahoma Medical Center. Dr. Whitsett's research is involved in cardiovascular and renal effects of autonomic and antihypertensive agents.

The Medical Student Traineeships in Clinical Pharmacology program provides opportunities to medical students to become aware of the basic techniques used in the field of clinical pharmacology. Hopefully, these students will sustain their interests in clinical pharmacology and choose this field as a career. This program provides a stipend of \$1,000 to each student for a three month period. A yearly fund of \$20,000 has been authorized for this program. Since 1967, when the first awards were made, 94 awards have been made to medical schools across the United States.



Geographical distribution of Foundation awards under the "Medical Student Traineeships in Clinical Pharmacology" program, 1967-1971.

- One
- More than one

The universities and students receiving awards in 1971 are:

University of California,
San Francisco
Steven Berkov
University of California, San Diego
Jeffrey N. Wilkins
Emory University
Robert J. Crisalli
Georgetown University
P. Lawrence Doebelin
Howard University
Nicholas A. Ongele
University of Maryland
M. Louis Offen
University of Minnesota
Gerald E. Merwin
Medical College of Pennsylvania
Paul L. Orr
University of Oregon
James L. Wilson
Temple University
Barry Slaven
Vanderbilt University
David H. Robertson
University of Vermont
Richard P. Lampert
Yale University
Irl Extein
Yale University
Dahlia Kirkpatrick

Information provided in 1971 from sponsors of 45 of the first 54 medical student trainees indicated that 30 students continued their interests in the field. Comments made by the sponsors of these students provide some interesting insights into the program. They indicated that it:

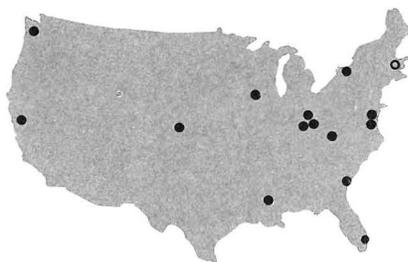
enhanced the ability of the clinical pharmacologist to attract students;

- fostered a sense of common purpose derived from clinical and basic science students working together under the sponsorship of the pharmaceutical industry;
- developed an above-average appreciation of clinical pharmacology and its value to the students' own specialties, even among those who do not plan to continue in the field;
- generated recognition by the student of the high-level support that pharmaceutical manufacturers provide in the common interest of improving the quality of therapeutics;
- was identified as a vital source of unrestricted support for medical students in clinical pharmacology in the United States.

Pharmacology-Morphology. *A post-doctoral program offered is the PMA Foundation Fellowship Awards in Pharmacology-Morphology.* Recent developments indicate the need for studies of drug-evoked changes in structure and their functional significance. The aim of the fellowships is to advance understanding of drug action through 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 and, in exceptional circumstances, may be extended for an additional year. The level of support is variable and is aimed at keeping within the existing stipend levels for similarly trained individuals within the applicant university. Since 1968 when the first fellowships were offered, 16 awards have been made.

The fellowship program is designed to support individuals trained to study the actions of drugs in relation to morphologic approaches (cytology, histology, ultrastructure, pathology). This pursuit applies an interdisciplinary training. Although the program requires that a candidate be qualified primarily either in a morphologic specialty or in pharmacology, training in the complementary discipline need not be formal. The aim is to have the candidate gain familiarity with a new disciplinary approach by using this primary discipline as a medium for acquiring the second. A yearly fund of \$70,000 has been set aside for this program.



Geographical distribution of Foundation "Fellowship Awards in Pharmacology-Morphology," 1968-1971.

- One
- More than one



Sharon E. Corey, Ph. D.



William A. Croft, Jr., D.V.M.



Penelope A. Fenner-Crisp, Ph. D.



Anita P. Hoffer, Ph. D.



Michael C. Lowe, Ph. D.



Asa K. Thureson-Klein, Ph. D.

Recipients of the wards which began July 1, 1971, are:

□ Sharon E. Corey, Ph. D., Medical Center, West Virginia University, Morgantown, W. Va. Dr. Corey will receive training in cell biology by using various methods including electron microscopy and cytochemistry. An epigenetic system in cell transformation will be used.

□ William A. Croft, Jr., D.V.M., Division of Clinical Oncology, University of Wisconsin, Madison, Wisconsin. Dr. Croft will study the pharmacology-morphology of thymic lymphoma induced in rats by a human cancer chemotherapeutic drug.

□ Penelope A. Fenner-Crisp, Ph.D., Department of Anatomy, School of Medicine-Dentistry, Georgetown University, Washington, D.C. Dr. Fenner-Crisp will study the effects of certain pharmacological and physiological substances upon fine structure morphology and the function of corpora lutea.

□ Anita P. Hoffer, Ph.D., Department of Anatomy, Harvard Medical School, Harvard University. Dr. Hoffer will extend her skills in electron microscopy and radioautography and apply them to the study of the site of action and ultrastructural effects of a variety of pharmacological agents which influence spermatogenesis, sperm release, and sperm maturation.

□ Michael C. Lowe, Ph.D., Department of Pathology, School of Medicine, University of Washington, Seattle. Dr. Lowe will study the mechanisms involved in the production of cardiomyopathies by catecholamines.

□ Asa K. Thureson-Klein, Ph. D., Department of Pharmacology and Toxicology Medical Center, University of Mississippi. Dr. Thureson-Klein will study noradrenaline storage vesicles of sympathetic nerves, stressing the pharmacological effects on the uptake, storage and release of catecholamines from the vesicles.

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

□ David W. Hiott, Ph. D., Department of Pharmacology, Medical College of South Carolina. He gained additional experience with the procedures of autoradiography and in certain techniques and interpretations of histochemistry, particularly at the electron microscopic level. His research efforts are directed toward the investigation of ultrastructural changes in the canine and hamster cardiac muscles by quinidine and daunomycin.

□ John O. Lindower, M.D., Ph. D., Department of Pharmacology, The Ohio State University. Dr. Lindower studied the effect of digitalis by correlating the changes the compound produces in heart cells. Isolated small animal hearts were perfused with the digitalis medium while a recording device measured the more forceful contraction that the drug produced in the heart. After the drug effect was demonstrated, small samples of the heart muscle were examined by the electron microscope to detect any changes that had been produced by the drug.

□ Timothy J. Mathew, M.B. B.S., Renal and Electrolyte Division, Georgetown University Hospital. He was engaged in studies directed to examination of platlets in the pathogenesis of transplant rejections. An attempt was made to alter histologic pattern rejection by using drugs directed at changing the platlet function. Following the conclusion of the fellowship, Dr. Mathew returned to Australia to assume responsibilities as Assistant Director, Renal Unit, Royal Melbourne Hospital.

Recipients of the awards which began July 1, 1969, are:

Andrew K. S. Ho, Ph.D., Department of Pharmacology, University of California, San Francisco Medical Center. Dr. Ho is extending his training through studies of the effect of cell structure and tissue function by the various psychopharmacologic drugs using a combination of techniques of electron microscopy, histochemistry and biochemical pharmacology. The findings are correlated to the therapeutic use of these drugs and their effect on behavior.

William J. Scott, Jr., D.V.M., Ph.D., Children's Hospital Research Foundation, Cincinnati, Ohio. The award enabled Dr. Scott to advance his training through a series of studies in rats and primates of the teratogenicity of a group of carbonic anhydrase inhibitors. His focus was on the mechanism of teratogenic action. In 1971 he accepted a position as Assistant Professor of Research Pediatrics at the University of Cincinnati.

Recipients of the awards which began July 1, 1970, are:

Roy J. Baerwald, Ph.D., Department of Medicine, University of Miami. Dr. Baerwald is investigating structural changes induced by such drugs as colchicine, vinblastine and vincristine in a range of invertebrate and vertebrate cells.

Patricia J. Bingham, D. Phil., Department of Pharmacology and Toxicology, University of Rochester.

Dr. Bingham is using autoradiography techniques to study the mechanism of action and localization of hormones and other agents which affect bone formation and resorption.

Richard F. Hoyt, Ph. D., Department of Pharmacology, Harvard School of Dental Medicine. He is studying the relationship between hormone and drug-induced changes in subcellular structure, particularly three strains of cultured mammalian tumor cells.

Carole Kimmel, Ph. D., in the Division of Toxicology, Kettering Laboratory Department of Environmental Health, College of Medicine, University of Cincinnati when the award was made. Dr. Kimmel studied the effects of betapropiolactone on the rabbit embryo and fetus to determine how this agent binds to DNA, RNA protein and other subcellular components, and any teratogenic or carcinogenic relationships. Dr. Kimmel has resigned the last three months of the fellowship and will assume responsibility for a research section in teratology, of the federal Environmental Protection Agency in Cincinnati.

Robert E. Seegmiller, Ph. D., Department of Molecular, Cellular and Developmental Biology, University of Colorado. Dr. Seegmiller is studying in mice the genetic-environmental interactions which influence the differentiation of cartilage and, subsequently, the morphology of limbs.

PUBLICATIONS

Drug Metabolism. A grant of \$12,500 was made to cover the preparation of a book entitled "The Fundamentals of Drug Metabolism and Drug Disposition". The contents of this book are updated versions of the presentations at three workshops on drug metabolism supported by the PMA Foundation in 1966, 1967 and 1968. Wider availability of the information presented at these workshops was considered highly desirable, since the meetings were limited to 40 participants each. The editors of the book are the directors of the 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 contributing authors in most instances are the members of the faculties at the three workshops. The Foundation cooperated with the Drug Research Board, National Academy of Sciences-National Research Council in the effort.

The book was published by The Williams and Wilkins Company in the fall of 1971 and has enjoyed wide acceptance. The initial printing of 3,500 copies has been exhausted and a second printing is underway. The contents of the 615 page book are divided into four parts: (1) Physical Properties of Drugs, Distribution and Excretion; (2) Drug Biotransformation: Environmental and Genetic Factors Which Modify Drug Metabolism; (3) Techniques for Studying Drug Biotransformation; and (4) Laboratory Experiments in the Study of Drug Metabolism and Drug Disposition.

Pharmacology Principles. A grant of \$12,000 beginning in 1971 was made to Ruth R. Levine, Ph.D., Professor of Pharmacology, Boston University of Medicine, to assist in the preparation of a textbook on the principles of pharmacology for use at the undergraduate level in the general curriculum of a college. The purpose of this textbook is to provide a concise source of the kind of pharmacologic knowledge that would be useful to anyone wishing to understand the ways in which chemicals interact with living organisms. It is being written primarily for the non-professional to provide the opportunity to acquire and share the basic information that will help him cope with a society where the use of drugs is constantly increasing and where exposure to chemicals can hardly be avoided.

The emphasis in the book is on the basic concepts and principles which are fundamental to understanding the action of drugs at any level of complexity. The biochemical and physiologic concepts needed to understand the pharmacologic principles will be an integral part of the text. Readers of diverse backgrounds need have in common only a working knowledge of general chemistry and biology. Hopefully, the availability of a textbook will serve the further purpose of implementing the presentation of courses in pharmacology in non-professional schools as part of a liberal arts curriculum.

The book will be in two volumes, the first covering topics in general pharmacodynamics and the second specific pharmacodynamics.

FOUNDATION FINANCES

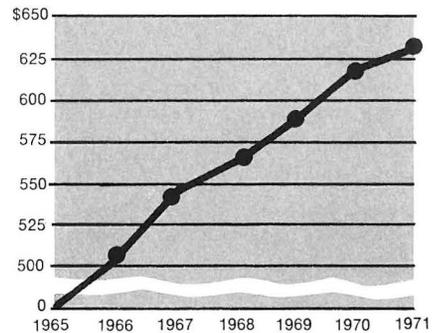
The Board of Directors of the Foundation decided at the outset that, as a minimum, total annual contributions of \$500,000 would be sought for each of the first three years of the Foundation's activities, extending through 1968, with larger amounts anticipated thereafter. For 1972 and each year until changed, the Board of Directors increased the contribution goal to \$750,000. In requests for voluntary support to 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. The total income in 1971 was \$702,820. Of this amount \$628,867 came from contributions. The balance of \$73,953 came from investments and refunds on unexpended balances from grants.

Contributions were received from approximately three of every four PMA Member Firms. About one half of the PMA Associates also joined in supporting the Foundation. Contributions were also received during 1971 from several individuals and groups in the health field.

Expenditures. Grants, Foundation-sponsored programs and administrative expenses for 1971 amount to \$620,104. Of this amount, \$542,069 represented expenditures for grants and Foundation-sponsored programs. There was a fund balance of \$890,361 as of December 31, 1971. This figure, however, does not reflect the tentatively authorized,

PMA Foundation Contribution Income 1965-1971 (Thousands)



undisbursed amounts 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, 1971, this contingency liability totaled \$854,669. Some of these grants represent amounts to be paid over the next two years. During 1972 the estimated amount to be paid on this tentative commitment is \$543,700.

Financial Reports. The Foundation's financial position as of December 31, 1971 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 to contributors quarterly during 1971. These reports are prepared by the Washington, D.C. accounting firm of Buchanan and Company. Quarterly reports will continue to be distributed to the Foundation's contributors during 1972.

STATEMENT OF INCOME AND EXPENDITURES

For the year ended December 31,
1971

Income

Contributions—Note a	\$628,867
Income from Investments	62,657
Miscellaneous Income	11,296
TOTAL INCOME	<u>\$702,820</u>

Expenditures

Grants—Note b

American Society of Pharmacology and Experimental Therapeutics— Supplemental Training	\$ 30,569
Boston University School of Medicine	12,000
Children's Hospital of Buffalo	22,297
Children's Hospital Research Foundation—Cincinnati	50,000
Clinical Pharmacology Faculty Program	110,269
Georgetown—Kidney Fund	20,000
Georgetown University School of Medicine	25,925
Hahnemann Medical College	15,000
Institute of Experimental Pathology and Toxicology	12,500
Medical College of Georgia	7,500
Medical Student Traineeships in Clinical Pharmacology	14,000
National Academy of Sciences	33,030
Pharmacology-Morphology Program	96,600
Rutgers—The State University	15,179
Stanford University Medical Center	15,000
Universities Associated for Research and Education in Pathology	12,500
University of Illinois, Urbana	3,000
University of Illinois at the Medical Center, Chicago	29,000
University of Oregon Dental School	2,700
University of Texas Southwestern Medical School at Dallas	15,000
	<u>\$542,069</u>
Administrative expenses	78,035
Total expenditures	<u>\$620,104</u>
Excess of income over expenditures	\$ 82,716
Fund balance at January 1, 1971	\$807,645
Fund balance at December 31, 1971	<u>\$890,361</u>

Note a—The Foundation received contributions of \$175,656 prior to December 31, 1971 which the Foundation considered applicable to 1972 and, therefore, are not recorded as income in 1971.

Note b—The Foundation has committed itself, subject to review, to make certain research grants. At December 31, 1971, the amounts still to be disbursed with respect to these grants aggregated \$854,669 of which approximately \$543,734 is expected to be disbursed during the year 1972. No liability has been reflected for these amounts at December 31, 1971.

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 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 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 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 16. General research support of the type described in the *Research* Section, pages 7-17, is still offered, but on a scale much reduced from that which has characterized the Foundation's earlier years. Therefore, while applications for general research support are accepted, the likelihood of support being granted is less than in the past.

These shifts in research support aim at providing an increase in the amount of educational funds available from the Foundation. The Foundation is expanding support within its current educational programs as outlined in the *Education and Training Programs* Section on page 18 and, when possible, will offer new programs already conceptualized, but awaiting funds.

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 operation funds were supplied by the PMA, and sustaining support for the Foundation has come from voluntary contributions from PMA Member Firms and Associates, industrial concerns, organizations and individuals with an interest in health care research.

ORGANIZATION AND ADMINISTRATION

The PMA Foundation operates through a Board of Directors and three advisory committees. The Chairman of the Board is H. W. Blades, Chairman of the Board, Wyeth Laboratories, C. Joseph Stetler is President, Raymond M. Rice, M.D. was Vice President until his retirement in December, 1971, and Thomas E. Hanrahan is Executive Director. In May, 1971, Mr. Blades was elected to succeed himself as Chairman of the Board; H. Robert Marschalk, President, Richardson-Merrell, Inc., was elected Vice Chairman and Daniel C. Searle, President and Chief Executive Officer, G. D. Searle & Co., was elected 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 three advisory committees.

The Scientific Advisory Committee has the responsibility of making recommendations to the Board of Directors on all general scientific grant requests and on the Research Starter Grants program. Irwin C. Winter, Ph. D., M.D., Vice President, Medical Affairs, G. D. Searle & Co., was Chairman of the committee until December, 1971. Earl Dearborn, Ph. D., M.D., President, Therapeutics Research Division, Dome Laboratories, was named Chairman to succeed Dr. Winter.

To increase its effectiveness, the Chairmen of the Medical and the Research and Development Sections of the PMA are invited to serve as 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 John A. Oates, M.D., Professor of Medicine and Pharmacology, Vanderbilt University, School of Medicine.

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

On July 4, 1971, the PMA Foundation lost a dedicated supporter. The sudden death of Dr. V. D. Mattia, President, Hoffmann-La Roche Inc., a member of the Board of Directors of the Foundation, left all with a sense of deep regret. His belief in the Foundation as an important institution in providing support within the biomedical sciences continues to motivate those entrusted to guide the development of the Foundation.

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* Retired December 14, 1971

† Deceased July 4, 1971

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It is suggested that requests for assistance take the form of a letter, outlining the subject, purposes, scope, brief description of methods or procedures to be used, principal researchers, percentage of time to be devoted to project by each of the principals, curriculum vitae, bibliographies of the principal researchers, the budget, other sources of present or anticipated financing of this same undertaking, a listing by title of other research projects presently involved in by the principal researchers and the amount of time devoted to each, and the amount and source of funds for these activities. All of the above information must be supplied.

In 1968, a policy was instituted which limits initial 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.

Letters should be addressed to:

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