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New Horizons in Medical Research

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A LARGE-SCALE, NATIONWIDE, peacetime program of support for scientific research in medical and related fields, guided by more than 250 leading scientists in 21 principal areas of medical research, is now a functioning reality. The program, based on U. S. Public Health Service Research Grants financed by public funds, supports research—conducted without governmental control—by independent scientists. The purpose of these grants is to stimulate research in medical and allied fields by making available funds for such research and by actively encouraging scientific investigation of specific problems on which scientists agree that urgently needed information is lacking. Accompanying this purpose is complete acceptance of a basic tenet of the philosophy upon which the scientific method rests: The integrity and independence of the research worker and his freedom from control, direction, regimentation, and outside interference.

The U. S. Public Health Service Research Grants, in operation as a medical research program of scientists and by scientists, may have early and profound effects upon the course of medical history and the national health.

The program, both in principle and as administered, has been welcomed and approved wholeheartedly by leaders in medical research. A total of 264 research projects, supported by $3,900,000 granted from the inception of the program late in 1945 up to 15 October 1946, already have been undertaken in 77 universities, hospitals, and other public and private institutions in 26 states. Although the program is less than a year old and has been little publicized, interest is rapidly widening, and new applications already are being received at a rate greater than 800 per year.

It is obvious that enormous savings of public and private money would result from research leading to wholesale prevention or cure of cancer, tuberculosis, diabetes, chronic nephritis, pernicious anemia, mental disorders, the common cold, heart diseases, and other widespread ailments.

Medical research costs money, however, and in the past a large amount of potentially very important research has not been conducted because funds have not been available to pay for it. Many universities and other nonprofit institutions have extremely limited funds for research, even though their teaching staffs, graduate students, and other personnel have the talent, training, and interest necessary for scientific investigation. Although research conducted by industrial organizations does add considerably to the total fund of medical knowledge, such research quite often must be directed toward specific goals.

The great benefits from all medical research, wherever conducted, are received by the millions of people whose lives are made healthier, happier, and longer through widespread application of knowledge gained in research laboratories. Conversely, research not conducted for want of funds is very costly to the same millions. The essence of these facts, as related to the Research Grants program, has been stated by the National Health Advisory Council: "There are few purposes for which public funds could be used more appropriately than to discover ways to prevent and cure illness and to prolong useful years of life." The function of the Research Grants is to make it possible for workers in medical and allied sciences to expedite, extend, and intensify health-saving and life-saving research.

During the war it frequently was necessary to sacrifice fundamental, not immediately applicable research in order to arrive at specific objectives promptly; promising bypaths often had to be by-passed. In the normal course of scientific investigation, however, the bypaths quite often lead to more important findings than do the roads from which they branch. Much of the most important research may not appear immediately to lend itself to clinical application, but it builds a large body of information, assembled parts from which may later have wide clinical applicability. The necessity for immediately restocking and enlarging the storehouse of fundamental data which forms the basis on which further advances in the medical sciences can be made is widely recognized, and the

opportunity to do this, curtailed during the war, is now greatly broadened.

In addition to research findings of immediate or ultimate applicability to the causes, diagnosis, treatment, and prevention of disease, benefits to be expected include an unprecedented opportunity to expand the Nation's resources in the fields of medical research. New nuclei of research can develop in universities, colleges, and other institutions which, heretofore, for want of funds, have been unduly limited in conducting scientific investigation. This expansion of activities in the field of medical research will provide training and experience for many promising young scientists and thus will enlarge significantly the ranks of qualified research workers necessary to carry on independently investigations in this field in the future. This aspect of the Research Grants supplements and complements the National Institute of Health Research Fellowships, which are described more fully in subsequent paragraphs.

Research Grants funds are *"additive"* and, as such, are intended to provide support for *additional* research—research that would not be conducted if additional funds were not available. They are not *"substitutive"* and therefore are not to be used to relieve a university or other institution of its financial responsibilities for usual or normal teaching, administrative, or research functions. Research Grants funds, however, may compensate for loss of teaching time if a substitute is employed to relieve the research director of normal teaching or administrative responsibilities, although supplementation of existing salaries cannot be provided. Furthermore, not more than 8 per cent—allowed only when fully justified—of the total amount of any grant may be budgeted for "overhead." Thus, the "additive" use of Research Grant funds does not in any way alter the financial structure of a participating institution.

Authority for the Research Grants

The Congress, in enacting Public Law 410, known as the Public Health Service Act, in 1944, stated the general powers and duties of the Public Health Service with respect to research and investigations. The law states that:

"The Surgeon General shall conduct in the Service, and encourage, cooperate with, and render assistance to other appropriate public authorities, scientific institutions, and scientists in the conduct of, and promote the coordination of, research, investigations, experiments, demonstrations, and studies relating to the causes, diagnosis, treatment, control, and prevention of the physical and mental diseases and impairments of man. . . ."

In carrying out the foregoing, the Surgeon General was authorized by the Congress in Public Law 410 and in amendments to "make grants in aid to universities, hospitals, laboratories, and other public or private institutions, and to individuals" for such research projects as are recommended by the National Advisory Health Council, the National Advisory Cancer Council, and the National Advisory Mental Health Council.

National Advisory Councils

These three Advisory Councils have been designated by the Congress to make recommendations to the Surgeon General of the U. S. Public Health Service regarding means necessary or appropriate to carry out his responsibilities with respect to research and investigations.

One of the important functions of the Councils is to act upon applications for Research Grants, with the advice and recommendation of special Study Sections composed of groups of scientists in the major categories of medical research.

The National Advisory Health Council consists of 14 members, 10 of whom are outstanding civilian scientists. The other experts are the director of the National Institute of Health and one representative each from the Army, the Navy, and the Bureau of Animal Industry as ex-officio members of the Council. This Council makes recommendations regarding all Research Grants except those relating specifically to research in the fields of cancer and mental health. Membership on this Council is for a period of five years; two new members are appointed each year to replace two retiring members.

The National Advisory Cancer Council, which, in addition to the Surgeon General, who serves as chairman, ex-officio, consists of 6 members selected from among leading medical and scientific authorities who are outstanding in the study, diagnosis, and treatment of cancer, reviews applications for Grants for research projects which show promise of making valuable contributions to the cause, prevention, or methods of diagnosis or treatment of cancer. Membership is for a period of three years; two new members are appointed each year to replace retiring members.

The National Mental Health Council consists of 7 members, including the Surgeon General, who is ex-officio chairman, and 6 members appointed from among leading medical or scientific authorities outstanding in the study, diagnosis, and treatment of psychiatric disorders. This Council reviews all applications for Research Grants for studies relating to the cause, prevention, and treatment of mental diseases. Membership is for three years, and two new members appointed each year replace retiring members.

Special Study Sections

At the request of the three Advisory Councils the fields of medical research were classified into major categories by the Research Grants Division of the

National Institute of Health. Special Study Sections made up of consultant experts in more than 20 major categories have been set up to provide the Advisory Councils with the benefit of their advice and judgment in passing upon applications for Research Grants. Members of the Study Sections include many of the Nation's outstanding research workers in medical and related sciences.

The special Study Sections have two major responsibilities: (1) to review applications for Research Grants in their respective fields, approving them, suggesting changes or further study, or disapproving them, and forwarding their recommendations to the appropriate National Advisory Councils; and (2) as scientific leaders, to survey the status of research in their fields in order to discern neglected areas in which research is particularly wanting, and to stimulate the interest of workers competent to undertake needed research.

Most Study Sections include a representative of the Army, the Navy, the Veterans Administration, and the Public Health Service.

The member from the Public Health Service serves as the executive secretary of each Section. Conferences of executive secretaries concerned are conducted whenever there is any question as to which Study Section should consider a particular application for a grant. If these executive secretaries decide that an application concerns more than one Study Section, the application is referred to one Section, which may seek advice of other Sections. Most Study Sections have regular quarterly meetings a few weeks in advance of the quarterly meeting of the National Advisory Councils.

Each Study Section, consisting essentially of outstanding civilian scientists, constitutes a scientific group with full authority and responsibility to make expert recommendation as to whether a research project application is acceptable and can be supported by Research Grants funds.

Study Sections inform workers in their respective fields, through announcements in appropriate professional journals or other publications, of the availability of Research Grants funds and of such other information as will further research in their fields.

Research Grants Division
The National Institute of Health

The Research Grants Division of the National Institute of Health was established late in 1945 to administer the Research Grants program of the U. S. Public Health Service. This Division is the administrative agent of the U. S. Public Health Service in relation to the National Advisory Health Council, National Advisory Cancer Council, and the National Mental Health Council. Applications for grants for research projects to be considered by any one of these three Councils, therefore, should be made to the Research Grants Division. When there is any question as to which Council should consider an application, this is solved by a meeting of the executive secretaries of the Study Sections set up under the various Councils. The principal responsibility of the Division is to conduct all administrative procedures in connection with Research Grants and to assist the special Study Sections and the National Advisory Councils in furthering medical research.

In addition to correlating and centralizing, in one office, administration of all Research Grants programs in the various Institutes and Divisions of the Public Health Service, the Research Grants Division is currently setting up a clearinghouse of data concerning medical research conducted under grant-in-aid programs of government, public, and privately financed agencies.

Kinds of Research Which May Be Conducted

Research "relating to the causes, diagnosis, treatment, control, and prevention of physical and mental diseases and impairments of man" falls within the scope of the Research Grants. Included is research in the fields of medicine, surgery, dentistry, antibiotics, bacteriology, biochemistry and nutrition, biophysics, cardiovascular diseases, endocrinology, gerontology, hematology, industrial diseases, malaria, pathology, pharmacology, physiology, public health methods, neurology, psychiatry, psychology, cancer, sanitation, venereal diseases, tropical diseases, virus and rickettsial diseases, and others.

In general, clinical work of a nonresearch character and nonmedical investigations in such fields as mathematics, physics, and chemistry are beyond the purposes of the program, although research projects in these fields may be conducted if they are considered likely to provide data applicable to medical science.

Whether a particular research proposal lies within these limits is determined by the appropriate special Study Section and National Advisory Council appraising the proposal.

Projects which are purely demonstrations of the application of epidemiologic, diagnostic, therapeutic, or preventive measures in the control of diseases do not qualify for Research Grants. (Aid for demonstration projects is provided by various divisions of the Public Health Service other than the Research Grants Division.)

A research project which has incidental demonstration aspects may be recommended for approval at the

discretion of the appropriate special Study Section and National Advisory Council.

Who May Apply for Research Grants

The Congress has authorized grants-in-aid for medical research to: universities, hospitals, laboratories, other public or private institutions, and individuals.

It is apparent that under the law no organization or individual is barred from applying for a grant-in-aid for research in a medical field. Although individuals may apply, the Research Grants Division encourages individual applicants to affiliate with a university, institution, laboratory, or other organization, since such affiliation greatly facilitates administration of grants, relieves the research worker of responsibility for bookkeeping and auditing, and provides him with better facilities than ordinarily would be available to an individual.

How Applications for Research Grants Are Made

Applications for grants-in-aid for medical research should be made on application forms available upon request from: Chief, Research Grants Division, National Institute of Health, Bethesda 14, Maryland.

Application forms provide for information regarding objectives of the proposed research, contemplated methods, and budget plan.

In order that administrative approval be indicated, an application made in the name of a university or other organization should be signed by an administrative official, such as the dean or president, rather than by the director of the project or departmental head.

The dean, department head, professor, or research director most familiar with the work of the applicant is requested to submit a letter giving his evaluation of the research proposal and of the investigator under whose immediate direction it is to be conducted.

The treasurer, bursar, or comptroller (by title) should be named as payee.

Applications may be submitted at any time, addressed to: Chief, Research Grants Division, National Institute of Health.

The Processing of Applications for Research Grants

Applications received by the Research Grants Division are reviewed by a special Study Section and a National Advisory Council.

Immediately upon receipt by the Division, each application for a grant-in-aid for medical research is duplicated, and a copy is forwarded promptly to each member of the special Study Section of experts in the field in which the proposed research lies. (Applications relating to research in the fields of cancer and mental health are forwarded by the Research Grants Division to the National Cancer Institute and the Mental Hygiene Division of the U. S. Public Health Service for submission to the appropriate Study Sections of the National Advisory Cancer Council and the National Advisory Mental Health Council.)

Each Study Section member, upon receiving an application forwarded to him, gives it preliminary consideration. If a Study Section member desires further information on a proposal, he may ask the Research Grants Division or the executive secretary of his Study Section to write the applicant, or, upon arrangement with the Study Section chairman, he personally may make direct inquiries or inspections.

At each regular or special meeting of a Study Section, all applications received since the previous meeting are formally considered without any priority ranking of research proposals.

Action by a special Study Section on a research proposal may consist of advising: (1) that it be accepted as submitted, (2) that it be rejected, or (3) that it be deferred pending further investigation or receipt of additional information. In advising any of these dispositions, Study Section members consider: (1) the scientific merits of the proposed research, (2) ability and training of investigator, (3) facilities available to investigator, and (4) such other considerations as the Section members regard as pertinent.

An application for a Research Grant is considered solely on the merits of the proposal; the applicant institution is not required to match any of the necessary funds requested.

After an application has been considered by a Study Section, it is forwarded with the Section's recommendation to the appropriate National Advisory Council for consideration at its next quarterly meeting. The advice of the Sections regarding applications usually is accepted by the Advisory Councils, but the latter are not obligated to accept this advice. If a Study Section disapproves an application, the Advisory Council, in all probability, will disapprove it also, and the applicant will be so advised. If the disapproving Study Section or Advisory Council indicates that a revision of the application might result in subsequent favorable action, the applicant is so informed.

All projects recommended by the Advisory Councils for approval are forwarded to the Surgeon General. After a research project has been approved by the Surgeon General, the applicant is notified and a check is sent to the payee. The research under an approved application may begin at any time in the year.

Since the Research Grants program is a peacetime program, emphasis is not placed on abnormal speed in conducting research. Research projects which will

take from three to five years or more may receive favorable consideration.

Grants of funds are made on a yearly basis; however, duration of the proposed investigation is an important consideration of the Study Sections and Advisory Councils in their decisions regarding recommendations for action. Approval of a project which the applicant has estimated will require more than a year to complete signifies a grant of funds for one year and an indication to the grantee of continued favorable action for as long as progress reports justify and Congress appropriates necessary funds. If a project requires more than one year to complete, a new application for continuation of the project must be submitted for each succeeding year; such renewal applications are processed in the same way as original applications.

An initially approved application is paid in full at the beginning of the first year. If an investigator needs additional funds during the year, he may file a supplementary application. If any funds remain unexpended at the end of a year, the amount given the investigator for the next year is adjusted. If any funds remain unexpended at the completion of a project, they are returned to the U. S. Government. Since any equipment or supplies purchased with Research Grants funds belong to the grantee rather than to the U. S. Government, no terminal accounting for such property is required.

How Research Is Conducted Under Research Grants

Research under the Research Grants program is conducted with full independence and autonomy of the research investigator. Support of research through the use of Research Grants funds does not imply in any way any degree of Federal control, supervision, or direction of the research project. The autonomy of the individual research worker implied in this philosophy, however, does not exclude self-imposed guidance entailed in the over-all plan of an organized, cooperative research project in which several groups of investigators may collaborate.

In order not to divert the time of the researcher unnecessarily from the actual conduct of the research investigation, only annual scientific progress reports are requested. It is not desired that the preparation of these reports present any long, tedious burden to the investigator, and it is therefore requested that they contain only such data in a brief, clear, and concise manner as will permit the appropriate Study Section and National Advisory Council to be adequately informed as to the conduct of the research investigations since the submission of the previous progress report. In this way the appropriate Study Section and National Advisory Council will be in a position to indorse the grant as it comes up for renewal annually. There may be certain instances in which a group of cooperative research investigators are concerned with a special problem of which interim reports are desired. These, however, are the exceptional instances.

Reports made to Study Sections are confidential and information from them is not circularized to other investigators without the consent of the grantee.

In order to avoid the possibility of restricting the autonomy of the research worker in any way, the Research Grants Division, the special Study Sections, and the National Advisory Councils will not review any papers proposed for publication, and therefore they are not in a position to indicate either approval or disapproval of such papers published solely at the election of, and under the complete control of, the research workers. This does not indicate any lack of interest in the results of research projects, but is aimed entirely at avoiding any degree of governmental restriction. After papers have been published, however, it is requested that the research workers provide the Research Grants Division with 50 reprints. It is also requested that published papers carry footnote acknowledgments of the Research Grant assistance from the Public Health Service.

Twice each year grantees submit simple financial reports to show current status of funds. The purpose of these reports is to facilitate routine auditing of Federal funds expended and to permit prompt regranting of any funds which may remain unused at the expiration of yearly grants.

National Institute of Health Research Fellowships

In order to further the development and training of competent research workers in the medical sciences and related fields, the National Institute of Health Research Fellowships program was established in 1945 under authority granted by the Congress in the Public Health Service Act.

Although this program is not administered by the Research Grants Division, its purposes are closely related to those of the Research Grants program.

The National Institute of Health Research Fellowships are awarded to individuals who have had post-graduate work in institutions of recognized standing in the various fields of medical and related sciences, such as biology, chemistry, physics, entomology, public health, medicine, dentistry, veterinary medicine, and others.

Applications for these fellowships may be made at any time during the year, are acted upon promptly, and are effective for one year from the time of award,

with a possibility of renewal for a second year.

Junior research fellowships are available to individuals holding Master's degrees or to those who have completed an equivalent number of hours of postgraduate study. The stipend is $2,400 per annum.

Senior research fellowships are available to individuals holding doctorate degrees. The stipend is $3,000 per annum. At the present time plans are being effected for the granting of fellowships to individuals at the level of B.S. or A.B. degree. The stipend likely will approximate $1,800 per annum.

These fellowships offer opportunities for study and research in association with highly trained specialists in candidates' chosen fields either at the National Institute of Health or any other approved institutions of higher learning. Letters of inquiry regarding them should be addressed to: The Director, National Institute of Health, Bethesda 14, Maryland.

Summary

From the above it is seen that the U. S. Public Health Service Research Grants program represents a sincere and continuing effort to supply Federal funds for the support of necessary additional research in the fields of medical and related sciences without interposing any degree of government restriction, control, supervision, or regimentation. The program is a scientific one, scientific guidance of which lies wholly in the hands of scientists.

Membership of National Advisory Councils

National Advisory Health Council

Gordon M. Fair, Graduate School of Engineering, Harvard University, Cambridge 38, Massachusetts.

Edwin B. Fred, University of Wisconsin, Bascom Hall, Madison, Wisconsin.

A. Baird Hastings, Department of Biological Chemistry, Harvard Medical School, Boston 15, Massachusetts.

Carl S. Marvel, 213 Noyes Laboratory, University of Illinois, Urbana, Illinois.

Kenneth F. Maxcy, School of Hygiene & Public Health, The Johns Hopkins University, 615 N. Wolfe Street, Baltimore 5, Maryland.

Karl F. Meyer, Director, The George Williams Hooper Foundation for Medical Research, University of California Medical Center, San Francisco 22, California.

John H. Musser, 1430 Tulane Avenue, New Orleans 13, Louisiana.

Harry S. Mustard, Columbia University School of Public Health, 600 West 168th Street, New York 32, New York.

William C. Rose, Noyes Laboratory of Chemistry, University of Illinois, Urbana, Illinois.

Henry F. Vaughan, Dean, School of Public Health, University of Michigan, Ann Arbor, Michigan.

(*Ex-Officio Members*)

Capt. O. L. Burton (MC), USN, Chief, Preventive Medicine Division, Bureau of Medicine & Surgery, Potomac Annex, Navy Department, Washington 25, D. C.

Assistant Surgeon General R. E. Dyer, Director, National Institute of Health, U. S. Public Health Service, Washington 14, D. C.

Col. Karl R. Lundeberg (MC), Chief, Preventive Medicine Division, Office of The Surgeon General, U. S. Army, Washington 25, D. C.

Harry W. Schoening, Chief, Pathological Division, Bureau of Animal Industry, U. S. Department of Agriculture, Washington 25, D. C.

National Advisory Cancer Council

Robert S. Stone, University of California Medical School, San Francisco 22, California.

Charles B. Huggins, Department of Surgery, University of Chicago, Chicago 37, Illinois.

George M. Smith, Yale University Medical School, 333 Cedar Street, New Haven, Connecticut.

Sherwood Moore, Director, Mallinckrodt Institute of Radiology, Washington University, St. Louis, Missouri.

Frank E. Adair, Memorial Hospital for the Treatment of Cancer and Allied Diseases, York Avenue and 68th Street, New York, New York.

A. C. Ivy, Northwestern University Medical School, Ward Memorial Building, 303 E. Chicago Avenue, Chicago 11, Illinois.

National Advisory Mental Health Council

Edward A. Strecker, Department of Psychiatry, University of Pennsylvania, 111 North 49th Street, Philadelphia, Pennsylvania.

William C. Menninger, Medical Director, Menninger Clinic, Topeka, Kansas.

John Romano, Professor of Psychiatry, School of Medicine, University of Rochester, Rochester, New York.

Frank F. Tallman, Commissioner of Mental Diseases, State of Ohio, State Office Building, Columbus, Ohio.

George S. Stevenson, Medical Director, National Committee for Mental Hygiene, 1790 Broadway, New York, New York.

David M. Levy, 300 Park Avenue, New York, New York.

Membership of Study Sections[1]

I. *Antibiotics Study Section*

Hans T. Clarke, Columbia University, *Chairman*; C. J. Van Slyke, National Institute of Health, *Executive Secretary*; David P. Barr, Cornell University; Robert D. Coghill, Abbott Laboratories; Vincent du Vigneaud, Cornell University; Harry Eagle, Johns Hopkins School of Hygiene; R. P. Herwick, Food and Drug Administration; Colin MacLeod, New York University; E. K. Marshall, Jr., Johns Hopkins University; J. E. Moore, Medical Arts Building, Baltimore; W. H. Peterson, University of Wisconsin; Milton V. Veldee, U. S. Public Health Service; Henry Welch, Food and Drug Administration; Oskar Wintersteiner, Squibb Institute for Medical Research; W. Barry Wood, Jr., Washington University; Maj. Ed-

[1] Additional Study Sections are being formed, membership of which will be announced when complete.

ward H. Vogel, Jr., U. S. Army; Capt. George B. Dowling, U. S. Navy; Arthur M. Walker, Veterans Administration.

II. *Bacteriology Study Section*

Gail M. Dack, University of Chicago, *Chairman*; C. L. Larson, National Institute of Health, *Executive Secretary*; William C. Boyd, Boston University School of Medicine; René Jules Dubos, Rockefeller Institute for Medical Research; William A. Hagan, Cornell University; Noel Paul Hudson, Ohio State University; W. H. Moursund, Baylor University; Stuart Mudd, Haverford, Pennsylvania; Walter J. Nungester, University of Michigan Medical School; Charles E. Smith, Stanford University School of Medicine; Selman A. Waksman, New Jersey Agricultural Experiment Station; Lt. Col. R. L. Cavenaugh, U. S. Army; Cdr. LeVerne A. Barnes, U. S. Navy; Leland Parr, Veterans Administration.

III. *Biochemistry and Nutrition Study Section*

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IV. *Cardiovascular Study Section*

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V. *Dental Study Section*

Paul C. Kitchin, Ohio State University College of Dentistry, *Chairman*; H. Trendley Dean, National Institute of Health, *Executive Secretary*; Hermann Becks, University of California; Harold C. Hodge, University of Rochester; George Paffenbarger, National Bureau of Standards; Isaac Schour, University of Illinois School of Dentistry; Lt. Col. Joseph L. Bernier, U. S. Army; Cdr. Carl A. Schlack (DC), U. S. Navy; Edwin M. Kennedy, Veterans Administration.

VI. *Gastric Cancer Study Section*

George M. Smith, Yale University, *Chairman*; Alexander Brunschwig, University of Chicago; Mandred W. Comfort, Mayo Clinic; Andrew C. Ivy, University of Illinois; Sherwood Moore, Washington University; George T. Pack, Memorial Hospital for the Treatment of Cancer and Allied Diseases, New York; Leonell C. Strong, Yale University; Owen H. Wangensteen, University of Minnesota; Shields Warren, New England Deaconess Hospital.

VII. *Gerontology Study Section*

Henry S. Simms, Columbia University, *Chairman*; Nathan W. Shock, National Institute of Health, *Executive Secretary*; Max A. Goldzieher, 104 East 40th Street, New York; Roy G. Hoskins, 25 Shattuck Street, Boston; Oscar J. Kaplan, San Diego State College; Clive M. McCay, Cornell University Agricultural Experiment Station; Wm. deB. MacNider, University of North Carolina; Robert A. Moore, Washington University School of Medicine; Capt. G. B. Tayloe (MC), U. S. Navy.

VIII. *Hematology Study Section*

Charles A. Doan, Ohio State University, *Chairman*; Kenneth M. Endicott, National Institute of Health, *Executive Secretary*; Edwin J. Cohn, Harvard Medical School; Henry N. Harkins, Johns Hopkins Hospital; Roy R. Kracke, University of Alabama Medical College; Carl V. Moore, Washington University School of Medicine; Joseph Stasney, Jefferson Medical College; M. M. Wintrobe, University of Utah; Col. William S. Stone, U. S. Army; Lt. Cdr. E. P. Cronkite, U. S. Navy; Francis P. Parker, Veterans Administration.

IX. *Malaria Study Section*

James A. Shannon, Squibb Institute for Medical Research, *Chairman*; G. Robert Coatney, National Institute of Health, *Executive Secretary*; G. A. Carden, Jr., New York City; L. T. Coggeshall, University of Chicago; A. C. Cope, Massachusetts Institute of Technology; Robert C. Elderfield, Columbia University; Clay G. Huff, University of Chicago; Robert F. Loeb, Columbia University; E. K. Marshall, Jr., Johns Hopkins University School of Medicine; Paul F. Russell, Rockefeller Foundation; Col. Karl R. Lundeberg, U. S. Army; Capt. James J. Sapero, U. S. Navy; E. A. Martin, Veterans Administration.

X. *Mental Health Study Section*

John Romano, University of Rochester School of Medicine, *Chairman*; Nolan D. C. Lewis, New York State Psychiatric Institute and Hospital, *Vice-Chairman*; Lawrence C. Kolb, U. S. Public Health Service, *Executive Secretary*; Philip Bard, Johns Hopkins University School of Medicine; Barney Brooks, Vanderbilt University; R. H. Felix, U. S. Public Health Service; Eugene B. Ferris, University of Cincinnati College of Medicine; Frank Fremont-Smith, Josiah Macy, Jr. Foundation; Thomas M. French, Institute of Psychoanalysis, Chicago; Roy Grinker, Michael Reese Hospital, Chicago; Charles A. Janeway, 721 Huntington Avenue, Boston; Kurt Lewin, Massachusetts Institute of Technology; Wm. Malamud, Worcester State Hospital; Margaret Mead, American Museum of Natural History; H. Houston Merritt, Montefiore Hospital, New York; I. Arthur Mirsky, May In-

stitute for Research, Cincinnati; Lucille Petry, U. S. Public Health Service; Marian C. Putnum, 37 Marlborough Street, Boston; David Rapaport, Menninger Clinic; Fritz Redl, Wayne University; George Richard Wendt, University of Rochester; Abner Wolf, Columbia University; Harold G. Wolff, Payne Whitney Psychiatric Clinic, New York; S. B. Wortis, Bellevue Hospital, New York.

XI. *Metabolism and Endocrinology Study Section*

Joseph H. Barach, University of Pittsburgh, *Chairman*; Hugh L. C. Wilkerson, Harvard School of Public Health, *Executive Secretary*; Jerome W. Conn, University of Michigan Medical School; Francis D. W. Lukens, University of Pennsylvania; Alexander Marble, 81 Bay State Road, Boston; Henry B. Mulholland, University of Virginia Hospital; Lester J. Palmer, The Mason Clinic, Seattle; Elaine P. Ralli, New York University College of Medicine; Henry T. Ricketts, University of Chicago; Randall G. Sprague, Mayo Clinic; Cecil Striker, 1019 Providence Bank Bldg., Cincinnati; Capt. W. F. Loftin (MC), U. S. Navy; Col. Charles R. Muller (MC), U. S. Army; Herbert M. Evans, Institute of Experimental Biology, University of California; Roy Hertz, National Cancer Institute.

XII. *Pathology Study Section*

Paul Cannon, University of Chicago, *Chairman*; R. D. Lillie, National Institute of Health, *Executive Secretary*; W. A. DeMonbruen, Nashville General Hospital; William H. Feldman, The Mayo Foundation; Wiley D. Forbus, Duke University; Harry Goldblatt, Cedars of Lebanon Hospital, Los Angeles; J. S. McCartney, University of Minnesota; Alan R. Mortiz, Harvard Medical School; Arnold Rich, Johns Hopkins University; James F. Rinehart, University of California; H. P. Smith, Columbia University; Col. Raymond A. Dart, U. S. Army; Cdr. R. V. Williams, U. S. Navy; C. E. DeAngelis, Veterans Administration.

XIII. *Pharmacology Study Section*

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XIV. *Physiology Study Section*

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XV. *Public Health Methods Study Section*

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XVII. *Sanitation Study Section*

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XVIII. *Surgery Study Section*

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XIX. *Syphilis Study Section*

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XX. *Tropical Diseases Study Section*

Andrew J. Warren, Rockefeller Foundation, *Chairman*; Willard H. Wright, National Institute of Health, *Executive Secretary*; Ernest Carroll Faust, Tulane University School of Medicine; William W. Frye, Vanderbilt University School of Medicine; John F. Kessel, University of Southern California; Henry E. Meleney, New York University College of Medicine; Gilbert F. Otto, Johns Hopkins University; Cornelius B. Philip, Rocky Mountain Laboratory, Hamilton, Montana; Albert B. Sabin, Children's Hospital Research Foundation, Cincinnati; Wilson G. Smillie, Cornell University Medical College; Col. Karl R. Lundeberg (MC), U. S. Army; Capt. J. J. Sapero (MC), U. S. Navy; Brig. Gen. James S. Simmons, Veterans Administration.

XXI. *Virus and Rickettsial Study Section*

John R. Paul, Yale University, *Chairman*; Norman H. Topping, National Institute of Health, *Executive Secretary*; Charles Armstrong, National Institute of Health; P. F. Clark, University of Wisconsin; John F. Enders, Harvard Medical School; Ernest Goodpasture, Vanderbilt University School of Medicine; Robert G. Green, University of Minnesota Medical School; Wm. McDowell Hammon, University of California; Geoffrey W. Rake, Squibb Institute for Medical Research; T. F. Sellers, Georgia State Department of Public Health; J. C. Snyder, Harvard School of Public Health; Max Theiler, Rockefeller Institute for Medical Research; Joseph E. Smadel, U. S. Army; Capt. James J. Sapero (MC), U. S. Navy.

Technical Papers

A Toxicity Study of Thiamine Hydrochloride

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Reingold and Webb (*5*) have recently reported that death occurred after four intravenous injections of thiamine hydrochloride (100 mg./cc.) into a human. These injections were given over a period of about one month, and it was concluded that death was due to anaphylaxis. However, the symptoms described were similar to those seen in this laboratory when a similar solution was injected intravenously into rabbits. In our work a 200- to 300-mg. total dose of thiamine usually resulted in collapse and/or death in most of the animals. If the injection was stopped before respiration ceased, the animal usually recovered within five minutes and apparently suffered no ill effects. These results were obtained over a period of eight months using 20 animals of about 3 kg. body weight. Hecht and Weese (*2*), in 1937, reported that the intravenous injection of 80 mg./kg. of thiamine hydrochloride caused no ill effects but that 160 mg./kg. caused death by paralysis of the central nervous system. Stern (*7*), in 1938, reported that death occurred in a cat given 20,000 I.U. of thiamine hydrochloride by cisternal puncture. Evidence has been presented that anaphylaxis and sensitivity both play a part in human thiamine hydrochloride toxicity (*1, 3, 4, 6, 8*).

Anaphylaxis in the rabbit is entirely different from that seen in the guinea pig or in humans. The lungs are not directly involved. The pulmonary artery is constricted, and the right auricle is engorged with blood. Respiration continues after cardiac arrest (*9*).

A group of five virgin female rabbits weighing between 1.5 and 1.9 kg. was given intravenous injections of a solution containing 100 mg./cc. of thiamine at the rate of 1 cc. every two minutes. Another group of five animals was given similar injections of a 0.35-per cent chlorobutanol solution. The solutions were given in this manner to determine which chemical was the cause of toxic manifestations seen when a solution containing 100 mg./cc. of thiamine hydrochloride and 0.35 per cent chlorobutanol (the usual commercial strength) was injected intravenously. The results of the thiamine injections are shown in Table 1. Each of the rabbits in the second group received 35 mg. of chlorobutanol (10 cc. of solution) and, when observed