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AMERICAN HEART ASSOCIATION, INC.

1775 Broadway, New York 19, N. Y.

APPLICATION FOR GRANT
(Original and 25 mimeographed copies to be submitted)

Medical Director
American Heart Association, Inc.
1775 Broadway
New York 19, N. Y.

Date October 30, 1951

Application is hereby made for a grant in the amount of \$12,100.00 for the period from July 1, 1952 to June 30, 1954 inclusive, for the support of research on the following subject:

A Study of the Serial Changes of Blood Volume and Body Water in Congestive Heart Failure.

Nathaniel I. Berlin, M. D. Lecturer and Research Associate in Medical Physics
John H. Lawrence, M. D. Director of Donner Laboratory of Medical Physics
(Name of Responsible Investigator)

Donner Laboratory of Medical Physics
(Address of Responsible Investigator)

University of California, Berkeley 4, California
(Institution where work is to be done) (Address)

Mr. James H. Corley, Vice President Business Affairs, University of California,
Berkeley 4, California

Give name and title of responsible institutional financial officer to whom funds should be sent and who will keep full and accurate account of disbursements.

It is understood that any grant made as a result of this request will be awarded on the following conditions: (1) the sum granted will be expended for the support of the research described above, except such an amount as may be designated by the American Heart Association for overhead expenses; (2) annual reports of expenditures and of work accomplished under a grant will be furnished to the Medical Director by a responsible institutional financial officer and the responsible investigator, respectively; (3) all reports of work accomplished with the support of a grant will acknowledge such support; (4) all discoveries which arise from work supported in whole or in part by a grant will be fully published in the usual scientific channels and will not be subject to patent; (5) if the responsible investigator leaves the institution before the expiration of a grant, the grant will terminate, unless arrangements satisfactory to the American Heart Association have been made; (6) at the end of the period covered by a grant, or when a grant otherwise terminates, the unexpended balance of the sum granted will revert to the American Heart Association (with due allowance for prior obligations), unless a further grant is made in support of the same program. The institution in the name of which this request is made is organized for scientific, educational and humanitarian purposes and is not a profit-making organization.

Approved by Executive Officer of the Agency or Institution under whose auspices the program is to be carried out.

s/ John H. Lawrence
s/ Nathaniel I. Berlin
Signature of Responsible Investigator

Name of Institution

Signature

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2. State the names and positions of individuals who are expected to assist in the proposed work in important capacities, as (a) consultants, or (b) research associates or assistants, or (c) others. (Whenever \$2,500 or more per annum is requested for professional personnel, the name of the person and his curriculum vitae should be attached.)

- Dr. G. M. Hyde, Research Fellow in Medical Physics, University of California.
- Dr. Sven G. L. Hedlund, Chief Assistant of the Cardiovascular Clinic of Sodertjukhuset, Rockefeller Foundation Fellow, Sodertjukhuset Stockholm, Sweden.

3. State briefly the facilities available for the proposed research.

The facilities are those of the Donner Laboratory of Medical Physics, University of California, and include all the major equipment necessary for this study. Out-patient facilities are available at the Donner Clinic and in-patient facilities, including a laboratory, are available at the Highland-Alameda County Hospital, Oakland, California.

4. For the support of the proposed research (give sources and amounts).
- a) what funds are now available?
NONE
 - b) what applications are pending?
NONE

7. Give below the itemized budget for the sum requested.

Note that the total budget should not exceed \$10,000 for a calendar year, as grants in excess of this amount will not ordinarily be made.

Note that while salaries may be included for research associates or assistants, or other professional personnel, amounts in this category of \$2,500 per annum or over will not be granted except in unusual circumstances (see 4, page 3). The American Heart Association has an entirely separate fellowship program and such professional personnel should ordinarily apply for appropriate fellowships.

Note that when part of the salary of the responsible investigator is included, the provisions outlined in the Announcement of Grants will prevail. The necessary information should accompany the application. (See Announcement of Grant-in-Aid, page 4.)

Close adherence to the details of the budget will not be required.

If a grant is made, the Association will add to the basic amount 5 per cent for institutional overhead. This amount should not appear in the proposed budget.

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PROPOSED BUDGET

Item	1952 - 1953	1953 - 1954	TOTAL
Personnel (itemize) (See 4, page 2.)			
20% physician research	\$ 2,000	\$ 2,000	
50% technician blood vol.	1,500	1,500	
50% technician H ³	1,500	1,500	\$10,000
Equipment (itemize)			
NONE			
Supplies (itemize)			
Lab. Glassware	250	250	
Chemicals, including P ³² and H ³	400	400	1,300
Travel Expenses to attend national meetings.	400	400	800
Other Expenses (itemize)			
NONE			
TOTAL	\$ 6,050	\$ 6,050	\$12,100

8. If this request is for renewal of a current grant, state the unexpected balance, if any, estimated to remain available at the end of the current grant.

NONE

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1. Outline of Proposed Research

Three groups of patients will be studied. The first will consist of patients with congestive heart failure resulting from arteriosclerotic or hypertensive cardiovascular disease; the second group will be those in failure as a result of rheumatic valvular disease; the third group will be patients with rheumatic valvular disease who have never been in congestive heart failure.

On admission a history will be obtained, a physical examination and the usual laboratory examinations will be carried out. In addition the blood volume will be determined with P^{32} labeled red blood cells, and the total body water with radioactive water (tritium). These patients will then be treated with the conventional methods of therapy for congestive heart failure, depending upon their clinical status. The patients will be followed carefully clinically, and the blood volume and body water studies repeated at intervals of approximately seven days until the patient is compensated. After compensation the patients will be seen at one month intervals, and the studies of blood volume and body water repeated as indicated by their clinical status.

The blood volume will be determined with P^{32} labeled red cells using the method of Kovesy and Zerahn as modified in this laboratory. Total body water will be determined with radioactive water by a method devised in this laboratory utilizing tritium. At the present time the equipment necessary for measuring body specific gravity and body volume is almost complete. When possible the patients being investigated in this study will have body specific gravity and body volume measurements with this equipment when their clinical condition permits. This will permit the determination of "fat free" body mass and consequently furnish a more precise index for the comparison of blood volume and body water with normals.

It is estimated that this project will require two years.

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2. a. Nathaniel I. Berlin, M. D.

Educated public schools of New York and Miami Beach, Florida, B. S. Western Reserve University 1942, M. D. Long Island College of Medicine, 1945, Ph. D. in Medical Physics, University of California, Berkeley, 1949. Intern, (1945-1946) Resident Pathologist (1946-1947) Kings County Hospital, Brooklyn, New York. National Cancer Institute Postdoctorate Research Fellow 1948-1950. Graduate student (1947-1949); Research Fellow in Medical Physics (1949-1950); Research Associate in Medical Physics 1950. Instructor and Research Associate in Medical Physics Jan. - July, 1951; Lecturer and Research Associate in Medical Physics July 1951, University of California, Berkeley, California.

John H. Lawrence, M. D.

Born Educated public schools of South Dakota. A. B. University of South Dakota, 1926; D. Sc. (Honorary) 1942. M. D. Harvard Medical School 1930. Formerly Instructor in Medicine, Yale Medical School; Intern and Resident training Peter Bent Brigham Hospital, Boston, Strong Memorial Hospital, Rochester and New Haven Hospital, New Haven. Professor of Medical Physics, Director, Donner Laboratory of Medical Physics, University of California, Berkeley.

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2. b. Previous work in this field done by chief investigator and associates.

Previous work on this and related problems has been the study of blood volumes in various disease states using P³² labeled red blood cells and studies using tritium to determine total body water. In addition, preliminary studies on the blood volume in congestive heart failure have been carried out. The work to date has shown that in congestive heart failure arising in patients with arteriosclerotic or hypertensive cardiovascular disease, the blood volume is normal, while in patients with congestive heart failure resulting from rheumatic heart disease, the blood volume was found to be considerably elevated.

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2. e. A study of serial changes of blood volume and body water in congestive heart failure.

This research project will consist of a study of three groups of patients, one with congestive heart failure resulting from artero-sclerosis or hypertensive cardiovascular disease; a second group will be those in failure as a result of rheumatic valvular disease; and a third group those with rheumatic valvular disease who have never been in failure. These patients will be studied in the following manner: in addition to the usual history and physical examinations, the blood volume will be determined with P³² labeled red blood cells and the body water will be determined with radioactive water (tritium). Patients will be treated and the changes in the blood volume and body water determined during the course of therapy. Following the completion of therapy the patients will be followed at intervals of one month and restudied if they again go into failure.