

University of California at Berkeley The Bancroft Library/The University Archives, Berkeley CA	
RECORDS SERIES TITLE	1165852
BANCROFT WARC ID NO.	1165
CARTON NO.	811
FOUNDER NAME	425 H. Fisher S
NOTES	11/21/11
FOUND BY/DATE FOUND	11/25/95

COPY

723317

SAN FRANCISCO: UNIVERSITY OF CALIFORNIA MEDICAL CENTER

BEST COPY AVAILABLE

October 12, 1954

John B. Lagen, M.D.  
Associate Dean  
University of California  
School of Medicine

Dear Doctor Lagen:

I attach an Application for a Grant-in-Aid to the American Heart Association submitted by Doctor I. S. Edelman for the support of research on, "Fluid and Electrolyte Anatomy in Patients with Essential Hypertension" in the amount of \$24,450.00 for the period July 1, 1955 to June 30, 1958.

Space and facilities are available to carry on this work in the Metabolic-Isotope Laboratories at the San Francisco City and County Hospital.

Sufficient copies of this request for all concerned are attached as well as thirty extra mimeographed copies which are to be submitted with the original application. In addition, I attach a statement in nontechnical language describing the nature and purpose of this project and a work sheet of the proposed research project.

This application meets with my entire approval.

Sincerely,

T. L. Althausen, M.D.  
Professor of Medicine  
Chairman, Department of Medicine

TLA:pan

Encs.

1165852

DOCUMENT SOURCE  
 University of California at Berkeley  
 The Bancroft Library/The University Archives, Berkeley CA

RECORDS SERIES TITLE  
 CA. WAIN. PHS. CORRISP. + PAPERS

BANCROFT/ARC ID NO.  
 1165

CARTON NO.  
 871

FOLDER NAME  
 285 H Folder 2

NOTE  
 P. 3/11

FOUND BY/DATE FOUND  
 H. H. G. 11/25/75

COPY

PROPOSED BUDGET

ITEM	1955-56	1956-57	1957-58	TOTAL
<b>PERSONNEL (itemize)</b>				
Senior Technician	4,092.00	4,296.00	4,512.00	
<b>EQUIPMENT (itemize)</b>				
2 microburettes	100.00			
Distillation glassware	500.00			
<b>SUPPLIES (itemize major purchases).</b>				
Isotopes (K <sup>42</sup> , Na <sup>24</sup> , Br <sup>85</sup> , D <sub>2</sub> O)	2,000.00	2,000.00	2,000.00	
Reagents and Expendibles	1,000.00	1,000.00	1,000.00	
<b>TRAVEL EXPENSES</b>	350.00	350.00	350.00	
<b>OTHER EXPENSES (itemize)</b>				
Repair and maintenance of Equipment	300.00	300.00	300.00	
<b>TOTAL</b>	<b>8,342.00</b>	<b>7,946.00</b>	<b>8,162.00</b>	<b>\$24,450.00</b>

1165833

UNIVERSITY SOURCE	
University of California at Berkeley The Bancroft Library/The University Archives, Berkeley CA	
RECORDS SERIES TITLE	112. UNIV PRES JAYISPARADUS
BANCROFT/MARC ID NO.	1123
CARTON NO.	871
FOLDER NAME	415 H.P. 1123
NOTES	D-111
FOUND BY/DATE FOUND	J. H. GILMAN 11/25/95

#### CURRICULUM VITAE

The curriculum vitae of the responsible investigator is on file with the American Heart Association since he is an Established Investigator of the American Heart Association.

#### Partial Bibliography

1. Weston, R. E., Hellman, L., Edelman, I. S., Grossman, J., and Leiter, L.: Studies on the Influence of the Low Sodium Cardiac Diet and the Kempner Regimen on Renal Hemodynamics and Electrolyte Excretion in Hypertensive Subjects. *J. Clin. Invest.*, 29:639, 1950.
2. Edelman, I. S., Olney, J. M., James, A. H., and Moore, F. D.: Studies on Total Body Composition by the Dilution Principle. *Science*, 115:447, 1952.
3. Edelman, I. S., Haley, H. B., Schloerb, P. R., Sheldon, D. B., Friis-Hansen, B., Stoll, G., and Moore, F. D.: Further Observations on Total Body Water. I. Total Body Water in the Normal Human Throughout the Life Span. *Surg., Gynec. & Obst.*, 95:1, 1952.
4. Edelman, I. S.: Exchange of Water Between Blood and Tissues. *Amer. J. Physiol.*, 171:279, 1952.
5. Cardozo, R. H., and Edelman, I. S.: The Volume of Dilution of Sodium Thiosulfate as a Measure of the Extracellular Fluid Space. *J. Clin. Invest.* 31:280, 1952.
6. Edelman, I. S., James, A. H., Brooks, L., and Moore, F. D.: Body Sodium and Potassium. V. Total Exchangeable Sodium; Normal Values and Methods of Measurement. *Metabolism*, In Press.
7. Moore, F. D., Edelman, I. S., Olney, J. M., James, A. H., Brooks, L. and Wilson, G. M.: Body Sodium and Potassium. III Interrelated Trends in Alimentary, Renal and Cardiovascular Disease. *Metabolism* 3:334, 1954.

1165834

DOCUMENT SOURCE	
University of California at Berkeley The Bancroft Library/The University Archives, Berkeley CA	
RECORDS SERIES TITLE	W. W. P. S. J. H. S. P.
BANCROFT/UA/UC ID NO.	11-5
CARTON NO.	371
FOLDER NAME	455 H. F. F. J. S.
NOTES	P. 5/11
FOUND BY/DATE FOUND	K. Traugott 12/19/55

COPY

**PROPOSED RESEARCH**

**A. Previous Work by Responsible Investigator in this Field.**

Studies on normal body composition by the isotope dilution method have been previously reported. These studies included measurements of total body water in normal human subjects (Edelman et al, S.G.O. 1952); measurements of total exchangeable potassium in normal human subjects (Edelman et al, Science, 1952); and measurements of total exchangeable sodium in normal human subjects (Edelman et al, Metabolism, In Press). A simplified technique for estimating the quantity of extracellular fluid was described (Cardozo and Edelman, J. Clin. Invest. 1952). An earlier work was devoted to a study on electrolyte excretion and renal hemodynamic changes induced by three levels of dietary sodium intake in hypertensive subjects (Weston et al, J. Clin. Invest. 1950). More recently an exploratory inquiry was made into body sodium and potassium contents in patients with alimentary, renal, and cardiovascular disease, including hypertension, (Moore et al, Metabolism 1954).

**B. Historical Background**

There are several lines of evidence implicating abnormalities in fluid and electrolyte metabolism in either the genesis or maintenance of essential hypertension. The administration of excessive amounts of sodium will produce hypertension in the rat and accentuate renal hypertension. Recently evidence has been obtained that the extracellular fluid volume as measured by the radio-sulfate space is increased in patients with essential hypertension. In addition many patients experience a lowering of blood pressure when placed on very low sodium intakes. Finally, potassium depletion appears to alter vascular reactivity significantly in the rat.

However, it may be that sodium retention and potassium depletion are secondary consequences of cardio-renal failure and not directly related to the genesis of human hypertension. It has been observed in a study of patients with essential hypertension that reduction in blood pressure did not correlate temporally with sodium balance. In a small series of patients with fairly severe hypertension, exchangeable sodium content was within the normal range. The purpose of this project is to characterize body composition with respect to water and electrolytes in patients with uncomplicated essential hypertension.

**C. Materials and Methods**

Three groups of subjects will be studied. A normal control group will consist of patients without hypertension or cardio-renal disease. The second group is to include only patients with uncomplicated essential hypertension prior to any therapy. The third group is to consist of hypertensives on diets adequate in caloric intake and unrestricted in sodium content treated with antihypertensive agents. Whenever possible the same patients will be studied in groups II and III.

Total exchangeable sodium, potassium and body water will be estimated by the isotope dilution method using Na<sup>24</sup>, K<sup>42</sup>, and D<sub>2</sub>O as tracers. Available extracellular fluid contents will be measured by thiosulfate dilution. At the same time, serum will be analyzed for, Na<sup>+</sup>, K<sup>+</sup>, Cl<sup>-</sup>, HCO<sub>3</sub><sup>-</sup>, pH and osmolarity. The methods to be employed

1165835

University of California at Berkeley The Bancroft Library/The University Archives, Berkeley CA	
RECORDS SERIES TITLE	ONLINE LIBRARY PAPER COPY/REPRODUCTION
BANCROFT/UA ARCH ID NO.	111-15
CARTON NO.	871
FOLDER NAME	415 H FOLDER 2
NOTES	3/4/11
FOUND BY/DATE FOUND	E. Mungier 1/25/75

COPY

SED RESEARCH (CONTD.)

re: Na<sup>+</sup> and K<sup>+</sup> by flame photometry, Cl<sup>-</sup> by electrometric titration, HCO<sub>3</sub><sup>-</sup> by Van Slyke, pH by meter and osmolarity by freezing point depression. It is anticipated that these data will enable us to determine whether (a) there are abnormalities in water and electrolyte anatomy early in the course of essential hypertension and (b) whether there are any changes in body composition that correlate with a positive or negative response to therapy.

4. SUMMARY OF THE RESEARCH PROJECT

Several lines of evidence implicate abnormalities in fluid and electrolyte metabolism in the genesis or maintenance of essential hypertension and experimental hypertension. A detailed study of water and electrolyte contents of human hypertensive subjects is still lacking. The proposed project is designed to meet this need and if possible supply answers to the questions of whether (a) there are abnormalities in water and electrolyte anatomy early in the course of essential hypertension and (b) whether there are any changes in body composition that correlate with the type of response to medical therapy.

The following measurements are contemplated:

- (1) Serum to be analyzed for Na, K, Cl, HCO<sub>3</sub>, pH and osmolarity.
- (2) Body composition to be defined with Na<sup>24</sup>, K<sup>42</sup>, D<sub>2</sub>O and thiosulfate. The simultaneous definition of body contents and serum concentrations should enable a more precise characterization of the interrelation between water and electrolyte metabolism and hypertension.

5. PERSONS FAMILIAR WITH WORK OF RESPONSIBLE INVESTIGATOR

- (1) Maurice Sokolow, M.D., Associate Professor of Medicine, University of California, School of Medicine, San Francisco 22, California.
- (2) Francis D. Moore, M.D., Professor of Surgery, Harvard Medical School and Surgeon-in-Chief, Peter Bent Brigham Hospital, Boston, Massachusetts.
- (3) Louis Leiter, M.D., Chief, Medical Division, Montefiore Hospital, New York 67, New York.

7. PARTICIPATING PERSONNEL

- (1) Judith Nadell, M.D., Research Fellow in Medicine, University of California, School of Medicine.
- (2) Lee W. Birkenfeld, M.D., Research Fellow in Medicine, University of California, School of Medicine.

1165836

