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Federal Security Agency
Public Health Service
National Institutes of Health
APPLICATION FOR RESEARCH GRANT

July 17, 1953

Public Health Service
National Institutes of Health
Bethesda 14, Maryland

Application is hereby made for a grant in the amount of 12, 561.48 for the period from April 1 1954 through March 31 1955 inclusive (not to exceed 1 year) for the purpose of conducting a research project on the following subject:

Title of Project Studies in neuromuscular diseases.

Name of Principal Investigator
William H. Blahd, M.D.

Augustus S. Rose, M.D.
(Clinical Consultant)

Title of Principal Investigator
Staff Physician, LAVA Hosp.
Clin. Inst. in Medicine, UCLA

Prof. of Med. (Neurology) UCLA

Address of Principal Investigator
School of Medicine
University of California Medical Center
Los Angeles 24, California

Name of Financial Officer to Whom Check Should be Mailed
George F. Taylor

Title of Financial Officer
Business Manager

Address of Financial Officer
Administration Building
405 Hilgard Ave.
Los Angeles 24, California

Name of Institution: University of California at Los Angeles

Name and Title of Official Authorized to Sign for Institution: Robert G. Sproul, President

Personal Signature: _____

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Budget Proposed for the Year April 1, 1954 through March 31, 1955

BUDGET

	Requested From P.H.S.	Other
Personnel:		
Senior Lab. Technician (Max Fields) full time	$ 3900.00	
Senior Lab. Technician (to be appt'd) full time	3900.00	
William H. Blahd, M.D., Principal Investigator	---	Full salary
Franz K. Bauer, M.D., Assoc. Investigator	---	" "
Raymond L. Libby, Ph.D., Assoc. Investigator	---	" "
Augustus S. Rose, M.D., Clinical Consultant	---	" "
Permanent Equipment:		
Chromatocab	275.00	
Densitometer	425.00	
Sewing machine, electric	75.00	
Mangle	75.00	
Hood installation	150.00	
Consumable Supplies:		
12 shipments of K^{42}	1200.00	
12 shipments of P^{32}	10.00	
Electronic equipment	200.00	
Chromatography supplies (solvents, paper, clips, sprayers)	150.00	
Pyrex jars, 10" (2)	36.50	
Glass racks (2)	32.50	
Travel:		
To attend medical conferences which pertain to this investigation.	500.00	
Other Expense:		
9% State Employees Retirement System	702.00	
Subtotal	11,631.00	
Overhead	930.48	
Total For The Year	12,561.48	

Estimate of Future Requirements

1. $ 13,000.00
2. 13,000.00
3. 13,000.00

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Public Health Service Support: Show previous and current Public Health Service grants supporting this project:

Previous

None

Current

None

All Other Support: Excluding Public Health Service, but including that from own institution, list support from other sources for this project; if none, so indicate

SOURCE	TITLE OF PROJECT	AMOUNT	PERIOD OF SUPPORT
Current			
Muscular Dystrophy Assoc. of America, Inc.	Study of muscular disorders by means of exchangeable radioactive potassium determinations.	$ 8,164.00	Oct. 1952 through Sept. 1953

Pending

None

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1. RESEARCH PLAN

A. Specific Aims--The proposed study is composed of three parts to be carried out concommitantly. (1) The determination of the total body potassium in the neuromuscular diseases with special reference to muscular dystrophy patients and their family members. (2) The study of amino-aciduria in patients having muscular dystrophy and other neuromuscular diseases by means of paper chromatography. (3) A study of the blood disappearance curve and urinary excretion of intravenously injected radioactive P^{32} in the neuromuscular diseases.

B. Method of Procedure--(1) Total body potassium will be determined by the technique of isotope dilution, using radioactive K^{42} according to the method described by Corsa et al., J. Clin. Invest., 29: 1280, 1950.

(2) Paper strip chromatography will be used to identify the constituent amino acids in the urine of patients having muscular dystrophy and other neuromuscular diseases. In addition, the excretion of radio-labelled amino acids will be studied by the paper chromatographic technique. The significance and implications of amino-aciduria in such patients will be evaluated by these and standard laboratory methods.

(3) Radioactive P^{32} will be injected intravenously and the blood disappearance curve will be plotted during the first 24 hours. An attempt will be made to correlate these data with the 24 hour excretion of P^{32} in the same patients.

All radioisotopes will be procurred either from Oak Ridge, Tennessee or accredited commercial sources. Dosimetry will be in accordance with the permissible dosage approved by the Subcommittee

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on Human Applications of the Atomic Energy Commission.

C. Significance of this Research--(1) Current work has indicated that total body potassium is diminished in cases of muscular dystrophy and myotonia atrophica, and this finding is manifest in very early cases. (See Sec. 3) The possibility of a family trait, characterized by diminished body potassium, must be considered.

(2) The existence of amino-aciduria in muscular dystrophy and other neuromuscular diseases has been known for some time. A detailed investigation of this condition has not been reported and may lead to a better understanding of these diseases.

(3) Recent work has suggested that there is a delayed disappearance curve of intravenously injected P^{32} in patients having neuromuscular diseases. This finding suggests the possibility that phosphorus distribution and metabolism is deranged in these diseases and requires further corroboration.

D. Facilities Available--The facilities of a fully equipped radioisotope laboratory in operation are available. In addition, the laboratory is equipped to do biochemical analyses required by the proposed research project with the exception of the equipment and materials requested above.

2. PREVIOUS WORK DONE ON THIS PROJECT

Work has been done in this laboratory which indicates that patients with muscular dystrophy and myotonia atrophica have diminished total body potassium. It has been demonstrated, furthermore, that this finding becomes manifest well before the full blown clinical picture. These results have been obtained from a study of 28 patients with neuromuscular diseases and 8 controls, using radioactive K^{42} and the dilution technique.

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Preliminary work has been done in this laboratory which suggests that there is a delayed disappearance curve of intravenously injected P^{32} in some patients with neuromuscular diseases despite what appears to be a normal excretion of this material.

3. PERSONAL PUBLICATIONS

Potassium Deficiency in Man, W. H. Blahd and S. H. Bassett. Metabolism, Clin. Exper., 2, No. 3, 218 (May) 1953.

Studies in Neuromuscular Diseases with Radioactive Potassium, W. H. Blahd, F. K. Bauer, R. L. Libby and A. S. Rose. (Presented before the 4th Annual Meeting, American Academy of Neurology, Chicago, April 10, 1953) In press - Neurology.

4. RESULTS OBTAINED BY OTHERS

Very little information is available concerning total body potassium levels in patients with neuromuscular diseases due to the newness of the technique for making this measurement. (Corsa et al.) Early work by J. N. Cummings on biopsy material revealed a diminished muscle potassium content in myotonia and an elevated potassium content in myasthenia. More recent work by Cannon et al. has demonstrated the essential nature of potassium in the synthesis of muscle protein.

Ames and Risley have demonstrated amino-aciduria in cases of muscular dystrophy. Further studies of amino acid excretion in such cases and other neuromuscular diseases have not been reported.

Corsa, L., Jr., Olney, J. M., Jr., Steenburg, R. W., Ball, M. R. and Moore, F. D., The Measurement of Exchangeable Potassium in Man by Isotope Dilution. J. Clin. Invest., 29: 1280, 1950.

Cummings, J. N., The Potassium Content of Muscle in Disease. Brain, 62: 153, 1939.

Cannon, P. R., Frazier, L. E. and Hughes, R. H., The Influence of Potassium on Tissue Protein Synthesis. Metabolism, 1: 49, 1952.

Ames, S. R. and Risley, H. A., Amino-aciduria in Progressive Muscular Dystrophy. Proc. Soc. Exper., Med. and Biol., 68: 131, 1948.

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BIOGRAPHY

William H. Blahd, M.D.

Age [redacted] [redacted] Citizenship: U.S.A.

August 1945 - M.D., Tulane University Medical School

1945-1946 - Internship, Kings County Hospital, Brooklyn

1946-1948 - U. S. Army, Capt. (MC)

1948-1951 - Residency, Internal Medicine, General Medical and Surgical Hospital, Veterans Administration Center, Los Angeles 25, California.

1951-1952 - Ward Officer, Metabolic Research Ward, Veterans Administration Center, Los Angeles 25, California.

1952 - Staff Physician, Radioisotope Unit, Veterans Administration Center, Los Angeles 25, California.

Clinical Instructor, Department of Medicine, University of California at Los Angeles.

Diplomate, American Board of Internal Medicine

Member: Alpha Omega Alpha
Los Angeles County Medical Association.

Publications:

Blahd, William H., Levy, Marvin S. and Bassett, Samuel H.: A Case of Hand-Schuller-Christian Syndrome Treated with Cortisone. Annals of Int. Med., 35: 927 (Oct.) 1951.

Blahd, William H., Adams, William S., Leslie, Alan, Goldman, Ralph and Bassett, Samuel H.: Electrolyte Changes Produced by ACTH, Cortisone, and Doca in Cirrhosis of the Liver, J. Lab. Clin. Med., 39: 393 (March) 1952.

Blahd, William H., Marcus, Raymond and Wasserman, David M.: A Case of Malignant Hypertension Secondary to Renal Ischemia, Annals of Int. Med., 37: 180 (July) 1952.

Adams, William S., Blahd, William H. and Bassett, Samuel H.: A Method of Human Plasmapheresis, Soc. Exper. Biology and Med., 80: 377, 1952.

Blahd, William H. and Bassett, Samuel H.: Potassium Deficiency in Man, Metabolism, Clin. Exper., 2, No. 3, 218 (May) 1953.

Leslie, Alan, Blahd, William H. and Adams, William S.: The Effect of Prolonged Administration of Epinephrine on Adrenal Cortical Function and Epinephrine Tolerance in Chronic Asthmatics, J. Lab. Clin. Med., 41: 865 (June) 1953.

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Blahd, William H., Bauer, Franz K., Libby, Raymond L. and Rose, Augustus S.: Studies in Neuromuscular Diseases with Radioactive Potassium, Neurology (In press).

Bauer, Franz K., Blahd, William H. and Fields, Max: Ascitic Fluid and Plasma Protein Exchange Studies with Radioiodinated Human Serum Albumin, J. Clin. Invest., 32: 553 (June) 1953. (Abstract)

Franz K. Bauer, M.D.

Age [redacted] [redacted] Citizenship: U.S.A.

M.D., Louisiana State University, School of Medicine, 1941.

Internship, Charity Hospital, New Orleans, 1941-1942.

Residency, Internal Medicine, Charity Hospital, New Orleans, 1942.

Army of the United States (Major, M.C.) 1942-1946.

Residency, Internal Medicine, Los Angeles County Hospital, 1946-1948.

Head Physician, Internal Medicine, Los Angeles County Hospital, 1949-1950.

Director, Radioisotope Unit, Wadsworth General Hospital, Veterans Administration Center, Los Angeles 25, Calif.

Assistant Clinical Professor of Medicine and Radiology, School of Medicine, University of California at Los Angeles.

Specialist, Certified by American Board of Internal Medicine.

Publications:

Goodwin, Wm. E., Bauer, Franz K., Barrett, Thomas F. and Cassen, Benedict: A Method using I^{131} for the Determination of Abnormal Thyroid Morphology, Am. J. Roentg. Rad. Therapy and Nuclear Med., 68, No. 6, 963 (Dec.) 1952.

Bauer, Franz K., Goodwin, Wm. E., Barrett, Thomas F., Libby, Raymond L. and Cassen, Benedict: Scintigrams of the Thyroid Gland. The Diagnosis of Morphologic Abnormalities with I^{131}. Calif. Med., 77: 380 (Dec.) 1952.

Bauer, Franz K., Cassen, Benedict, Youtcheff, Elsie and Shoop, Lucille: Jet Injection of Radioisotopes. A Clinical Study Comparing Needle and Jet Injection of I^{131}, K^{42} and Na^{24}. Am. J. Med. Sc., 225: 374 (April) 1953.

Bauer, Franz K. and Yuhl, Eric T.: Myelography by Means of I^{131}. The Myeloscintigram. Neurology, 3, No. 5, 341 (May) 1953.

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BIOGRAPHY

Raymond L. Libby, Ph.D.

Age [redacted] [redacted] Citizenship: U.S.A.

Ph.D., Rutgers University, New Brunswick, N.J., 1938
M.S., " " " " " 1937
B.A., " " " " " 1925

Scientific Director, Radioisotope Unit, Wadsworth General Hospital, Veterans Administration Center, Los Angeles 25, California.

Associate Professor of Radiology, School of Medicine, University of California at Los Angeles.

Member of:

Sigma Xi
The American Association of Immunologists
American Chemical Society
American Society of Zoologists
Society for Experimental Biology & Medicine
Elected Fellow of New York Academy of Science, 1948.

Past five publications (of a total of 25)

Libby, Raymond L., Taylor, Christine M., and Thomas, Panchita B.: Practical Aspects of Laboratory Scintillation Counting, J. Lab. Clin. Med., 40, No. 4, 641 (Oct.) 1952.

Libby, Raymond L., and Tubis, Manuel: Capsules for Oral Administration of Radioisotopes, Nucleonics, Vol. 10, No. 3, 63-64, 1952.

Allen, Herbert C., Jr., Libby, Raymond L. and Cassen, Benedict: The Scintillation Counter in Clinical Studies of Human Thyroid Physiology Using I^{131}, J. Clin. Endocrin., Vol. XI, No. 5, 492, 1951.

Cassen, Benedict, Curtis, Lawrence, Reed, Clifton and Libby, Raymond L.: Instrumentation for I^{131} Use in Medical Studies, Nucleonics, 9, 2, 46-50, 1951.

Fields, Max and Libby, Raymond L.: Uptake of Labeled Antigens by the Mitochondria of Mouse Liver, J. Immunology, 69, No. 6, 581 (Dec.) 1952.

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BIOGRAPHY

Augustus B. Rose, M.D.

Office Address: University of California Medical Center, Los Angeles 24

Home Address: 625 North Crescent Drive, Beverly Hills, California

Born: Fayetteville, North Carolina, July 14, 1907

Degrees:

B.S. in Medicine, University of North Carolina, 1930
M.D. Harvard, 1932

Certification:

American Board of Psychiatry and Neurology
Neurology--1940
Psychiatry--1942

Teaching and Research Positions:

Teaching Fellow in Anatomy, University of North Carolina, 1928--1930
Teaching Fellow in Histology, Harvard Medical School, 1931--1932
Associate Professor of Anatomy, University of North Carolina, 1934--1937
Assistant in, and Instructor in Neurology and Psychiatry, Harvard Medical School, 1937--1951
Professor of Medicine (Neurology), University of California at Los Angeles, 1951

Neurologist, Peter Bent Brigham Hospital and Massachusetts General Hospital, 1937--1951
Senior Psychiatrist, Boston Psychopathic Hospital, 1943--1951
Assistant, Associate and Chief--Dept. of Therapeutic Research, Boston Psychopathic Hospital, 1939--1951
Consultant in Neurology, Los Angeles Veterans Administration Hospital (Sawtelle), 1951--

List of Most Important Publications During the Past Five Years:

Rose, A. S.: An Outline for Diagnosis and Modern Treatment of Central Nervous System Syphilis. North Carolina Med. J., 8: 285-290, May, 1947.

Rose, A. S., Solomon, H. C. and Arnot, R.: Electric Shock Therapy in General Paresis. J. Nerv. & Ment. Dis., 107: 377-381, April, 1948

Chapman, W., Rose, A. S., and Solomon, H. C. Measurements of Heat Stimulus Producing Motor Withdrawal Reaction in Patients Following Frontal Lobotomy. The Frontal Lobes, research publication of the Association for Research in Nervous and Mental Diseases (ARNMD). Vol. XXVII, 1948, Baltimore, Md. Williams & Wilkins Co., Chapter 34, 754-768.

Rose, A. S. and Solomon, H. C.: Prefrontal Lobotomy: A Consideration of Unsuccessful Cases. Failures in Psychiatric Treatment, Ch. 12, 174-181, 1948

Rose A. S.: Some Observations on Lobotomized Patients Based Upon Routine Neurological Examinations. J. Nerv. & Ment. Dis., 109: 201-209, March, 1949

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Submitted to: Public Health Service, National Institutes of Health, Div. of Research Grants, Bethesda 14, Md.

Title of Project:

Studies in neuromuscular diseases.

Give Names, Departments, and Official Titles of Principal Investigator and All Other Professional Personnel:

W. H. Blahd, M.D.	Clin. Inst. in Med., UCLA	Staff Physician, LAVA Hosp.
F. K. Bauer, M.D.	Asst.Clin.Prof.Med./Rad., UCLA	Director, Radioisotope Unit, LAVA Hosp.
R. L. Libby, Ph.D.	Assoc. Prof. Radiology, UCLA	Scientific Director, Radioisotope Unit, LAVA Hosp.
A. S. Rose, M.D.	Prof. of Neurology, UCLA	Consultant in Neurology, LAVA Hosp.

Name and Address of Applicant Institution:

University of California at Los Angeles
Los Angeles 24, California

Summary of Proposed Work:

The proposed study is composed of three parts. (1) The investigation of total body potassium in family members of individuals afflicted with muscular dystrophy. Recent work in this laboratory indicates diminution of body potassium stores in patients having early, as well as advanced, muscular dystrophy. Total body potassium will be determined by the isotope dilution technique, using radioactive K^{42}. (2) Investigation of the aminoaciduria, observed by earlier workers, in patients having muscular dystrophy and other neuromuscular diseases, using the method of paper strip chromatography. Identification of individual constituent amino acids will be attempted, using radioactive labelled amino acids and standard laboratory techniques. (3) The blood disappearance curve of intravenously injected radioactive P^{32} will be studied in the various neuromuscular diseases. The correlation between blood disappearance and urine excretion of P^{32} in such patients will be investigated.

Signature of
Principal Investigator _____

Identify any professional School (Medical, Dental, Public Health, Graduate, or Other) with which this project should be identified.

University of California Medical Center (School of Medicine) Los Angeles 24, Calif.

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