

L. D. Mackay, Director
Finance Division

August 23, 1957

Herman M. Roth, Director
Research and Development Division

8/26
alice

CONTRACT NO. AT-(40-1)-1646 - DUKE UNIVERSITY

SYMBOL: ORS:JDB

This is to advise you that the work under Contract No. AT-(40-1)-1646 with Duke University has been completed and that an acceptable final report has been submitted. Therefore, the obligations of the University have been concluded and the contract should be closed out.

Original signed by

C. S. Shoup

for Herman M. Roth

cc: J. R. Moore ✓
F. E. McPherson

BEST COPY AVAILABLE

REPOSITORY *Oak Ridge Opr.*
Records Holding Area
COLLECTION *Documents 8944-94*
Contracts AT-(40-1)-1630-1646
BOX No. *1 of 1 Bldg. 2714-H*
Contract Correspondence
FOLDER *cont. AT-(40-1)-1646-Duke*

Res. Ser. Br. Res. & Dev.

381

Burleson:ji

In Reply Refer To:
ACG:JN

Oak Ridge, Tennessee
June 29, 1956

Duke University
Office of the Business Manager
and Comptroller
Durham, North Carolina

Attention: Mr. A. S. Brewer

Subject: MODIFICATION NO. 3 TO CONTRACT NO. AT-(10-1)-1646

Gentlemen:

Enclosed, in accordance with your letter dated June 25, 1956,
you will find one duly signed copy and two conformed copies of
Modification No. 3 to your Contract No. AT-(10-1)-1646.

Very truly yours,

John R. Moore
Director
Contract Division
Oak Ridge Operations


Enclosure;
Mod. 3 (in trip.)

Director

OFFICE ▶	Cont. Coord. Br.	Cont. Div.				
SURNAME ▶	Nicholson	Moore				
DATE ▶	6-29-56	6-29-56				

1110010

Duke University
DURHAM
NORTH CAROLINA

Office of the
Business Manager and Comptroller

June 25, 1956

United States Atomic Energy Commission
Oak Ridge
Tennessee

In Re: ACC: JN

Gentlemen:

Enclosed herewith I am returning two fully executed copies of Modification No. 3 to Contract No. AT-(40-1)-1646. One copy of this Modification is being retained in our office. As soon as this document has been approved on behalf of the Commission, we shall appreciate your sending us one (1) officially signed copy and two (2) conformed copies for use in our offices.

There are also enclosed two (2) copies of "Notice of Research Project" which have been signed by Dr. Jerome S. Harris, who is the Senior Investigator.

Yours very truly,



Business Manager and
Treasurer

ASB/td

Enc. *ASB/td*

CC: Dr. Jerome S. Harris

1110011

Mod. 3 to Cont. AT-(110-1)-1646

Duke University

Distributed June 28, 1956

Washington

Cont. files (2)

Finance

Res. and Development (2)

Wash. (B&M-2)

extra copies

1110012

Mod. 2 to Cont. AT-(40-1)-1646

Duke University

Distributed June 30, 1955

Washington

Cont. files (2)

Finance (2)

Res. & Medicine (2)

Wash. (B&M-2)

extra copies

1110013

Duke University
DURHAM
NORTH CAROLINA

Office of the
Business Manager and Comptroller

June 27, 1955

United States Atomic Energy Commission
Oak Ridge
Tennessee

In Re: ADC:JN

Gentlemen:

Enclosed herewith I am returning one fully executed copy of Modification No. 2 to Contract No. AT-(40-1)-1546. Two copies of this Modification are being retained in our offices.

There is also enclosed a "Notice of Research Project" which has been signed by Dr. Jerome S. Harris, who is the Senior Investigator.

Yours very truly,

(Signature)
Business Manager and
Comptroller

f d

ASE/ps
Encl.

CC: Dr. Jerome S. Harris

1110014

In Reply Refer To:
ACC:JN

Oak Ridge, Tennessee
June 20, 1956

Duke University
Department of Pediatrics
Durham, North Carolina

Attention: Mr. A. S. Brewer, Business Manager

Subject: MODIFICATION NO. 3 TO CONTRACT NO. AT-(40-1)-1646

Gentlemen:

Enclosed, in triplicate, is proposed Modification No. 3 to the subject contract which provides for an extension of the contract term to June 30, 1957. Also enclosed is a Notice of Research Project form which is to be used in submitting the summary statement.

If the modification, as submitted, is satisfactory to you it is requested that you secure the Senior Investigator's and the proper official of the University signature on two of the enclosed copies and return them to this office. The summary statement should be returned along with the signed copies of the modification. After signature on behalf of the Commission, one duly signed copy of the modification will be returned for your retention.

Very truly yours,

R. G. Humphries
Acting Director
Contract Division
Oak Ridge Operations


Enclosures:
Mod. 3 (in trip.)
Res. Project form

OK
CC: Dr. Shoup

		Acting Director			
OFFICE ▶	Cont. Coord. Br.	Cont. Div.			
SURNAME ▶	Nicholson: jn	Humphries			
DATE ▶	6-20-56	6-20-56			

1110015

Office Memorandum • UNITED STATES GOVERNMENT

TO : J. W. Ould, Jr., Assistant General Counsel

DATE: May 31, 1955

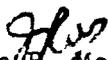
FROM : John R. Moore, Director, Contract Division

SUBJECT: RENEWAL OF CONTRACT NO. AT-(40-1)-1646 - DUKE UNIVERSITY

SYMBOL: ADC: HSH

Attached is an approved proposal for renewal of subject contract for a period of one year beginning July 1, 1955. This action is covered by Contract Authorization No. EM-55-341, dated April 29, 1955, in the amount of \$5,300.

Please prepare an appropriate modification to renew this contract for a period of one year, beginning July 1, 1955, with additional funds in the amount of \$5,300.


John R. Moore

Attachments:

1. Request for Contract Action
2. Budget for Contract AT-(40-1)-1646
3. Resume
4. Cy. ltr. from Shoup to Harris, dtd 5-24-55
5. Cy. memo from Roth to Bugher dtd 5-24-55
6. Contract Authorization No. EM-55-341
7. Cy. ltr. from Harris to Roth, dtd 5-17-55
w/Revised Budget
8. Renewal Application

CC: C. S. Shoup
L. D. MacKay
J. Nicholson w/Encls. 1 & 2

Hutchins:hsh

1110016

<p>6. Contract Board Docket No. _____ (To be assigned by Board Secretary)</p>	<p>7. Request Submitted By: (signed) _____ Date: <u>5-27-55</u> Title: _____ <i>Harman H. Kohn</i></p>
<p>8. Complete Description of Services to be Furnished by Contractor: Washington designated research contract. Title: "I. Metabolism and Physiological Role of Potassium; II. Metabolism of Renal Insufficiency." (If more space is required use separate sheets and attach hereto:)</p>	
<p>9. Description of other changes to be covered by Modification: Renew contract period for one year beginning July 1, 1955, with Commission funds in the amount of \$5,300. (If more space is required use separate sheets and attach hereto:)</p>	
<p>10. Negotiated Contracts. (Show why it appears desirable to negotiate new contract or to negotiate modification to existing contract) Memo from J. J. Hughes to S. R. Sapirie dated April 29, 1955. (If more space is required use separate sheets and attach hereto:)</p>	
<p>11. Contracts, Subcontracts, or Purchase Orders Submitted for Review and Approval: (Furnish brief descrip- tion of action in this space and attach pertinent documents) None</p>	
<p>12. Disputes: Attach a statement summarizing the dispute together with pertinent documents and Background Material. None</p>	

15317

1110017

1. Chairman
 TO: J. R. Moore Contract Board. From: Research Medicine Div.

It is requested that the Contract Board take the necessary action to process the following described contract action in accordance with the provisions of Bulletin OR-O&M-19:

2. Nature of Action Requested

Selection of New Contractor and Negotiation of Contract.

Modification of Contract
 No. AT-(10-1)-1646

Contractor: Duke University

Review and approval of Contract, Sub-contract or Purchase Order.

Other (Explain) Durham, North Carolina

Number: _____

Name: _____

3. Nature of Services to be Covered by Contract

Construction

Architect-Engineer

Other

(Explain) Research

4. Funding

Amount to be Obligated by this Contract Action \$ 5,300.

Source of Funds

Approved ORO Financial Plan, _____ Quarter, Fiscal Year 19__

Project No. _____ or, Activity No. 6300

Funds to be Obligated: Allotment No. 66-51-91/2 (F.Y. 1955 Funds)

Procurement Directive No. BM-55-391 Dated 4-29-55

Issuing Office Div. of Biology & Medicine

Concurrence in Funding Statement: (signed)

Joseph L. Petty
 Chief, Budget Branch 5/31/53

5. Project or Activity to be Covered by Contract Action:

Location of Work: _____ Construction Directive No. _____

Estimated Cost of Work to be Covered by this Contract Action \$ _____

Schedule: Date Work to Start _____ Estimated Completion Date _____

Description of Project or Activity:

(If more space is required use separate sheets and attach hereto:)

1110018

Budget For Contract No. 41-(43-1)-2446

For Period 7/1/57 - 6/30/58

1) <u>Salaries and Wages:</u>		11,710.00
Dr. J. S. Harris	\$2,500.00	
Other Faculty	1,500.00	
Research Assistants, Technicians, Etc.	4,500.00	
Secretarial Assistance	250.00	
2) <u>Equipment:</u>		750.00
3) <u>Supplies:</u>		1,000.00
4) <u>Travel and Communications:</u>		363.36
5) <u>Indirect Costs:</u> (36.37% of Salaries and Wages):		<u>3,132.37</u>
	TOTAL	14,045.73

The Commission's contribution to the above budget will be \$5,300; the contractor's contribution will be \$6,245.73; and \$2,500 is available from the previous period for use during this period.

DUKE UNIVERSITY SCHOOL OF MEDICINE,
DEPARTMENTS OF PEDIATRICS AND BIOCHEMISTRY,
DURHAM, NORTH CAROLINA.

CONTRACT NO. AT-(40-1)-1646.

DR. JEROME S. HARRIS,
Professor of Pediatrics and
Associate Professor of Biochemistry,
Project Leader.

STUDIES OF ELECTROLYTE AND FLUID BALANCE IN HEALTH
AND DISEASE.

RESUME'

The Contractor will
~~It is proposed to,~~ continue studies of cardiac muscle electrolyte metabolism and its relation to arrhythmia, particularly that caused by hypercapnia. Studies will be made on differences in the effects of potassium and carbon dioxide, and where practical the radioisotope Potassium-42 will be used. Chloride studies will be accomplished with $K^{42}Cl$. Studies of the metabolism of potassium will be made with particular reference to the problem of bound and non-exchangeable potassium and the nature of complexes which may be formed.

C. S. Shoup

1110020

In Reply
Refer to: 11:507

Oak Ridge, Tennessee
May 24, 1955

Dr. J. S. Harris
Department of Pediatrics
Duke University
Durham, North Carolina

Subject: CONTRACT NO. AT-(40-1)-1646

Dear Dr. Harris:

We have initiated action for the preparation of a modification to Contract No. AT-(40-1)-1646 to extend the period to June 30, 1956, with the Commission contributing \$5,300 in new funds to the total cost of \$14,045.73. A copy of the budget to be included in the modification is enclosed for your information. The modification will be mailed to you for signature as soon as it is complete. We shall appreciate your prompt attention to the modification when you receive it so we may receive our copies back as soon as possible.

You will note that the enclosed budget does not agree with the revised budget as submitted by your letter of May 17, 1955. In our letter of May 4, 1955, we inadvertently listed \$1,500 as being available from the previous period instead of the \$2,500 as pointed out in your letters of April 18 and May 5, 1955. Therefore, we recomputed the budget to include the extra \$1,000. In the event additional funds remain unexpended on June 30, they may be used under the contract.

Your cooperation in this matter is appreciated.

Very truly yours,

C. S. Shoup
Chief, Biology Branch
Research and Medicine Division

Enclosure:
Budget

CC: A. S. Brower, North Carolina
J. R. Moore ✓

Rounsaville:lr

1110021

J. C. Bugher, Director
Division of Biology and Medicine, Washington

May 24, 1955

Herman M. Roth, Director
Research and Medicine Division, Oak Ridge

CONTRACT NO. AT-(40-1)-1646 - DUKE UNIVERSITY

SYMBOL: OR:JLR

Reference is made to your memorandum of April 29, 1955, to S. R. Sapiro, symbol HM:PGL, approving the extension of Contract No. AT-(40-1)-1646.

In the renewal proposal, the contractor listed \$1,500 as available June 30, 1955, for use during the next period. We have been advised that \$2,500 will be available and have prepared the contract on the basis of \$5,300 in new funds from the Commission, \$2,500 available from the previous period, and a contribution of \$6,245.73 from the contractor. We trust this meets with your approval.

Herman M. Roth

CC: J. R. Moore ✓

Rounsaville:lr

1110022

May 17, 1955

RE: CR:JHR

Dr. Herman N. Roth, Director
Research and Medicine Division
United States Atomic Energy Commission
Oak Ridge, Tennessee

Dear Dr. Roth:

Enclosed is the revised budget for Contract #AT-(40-1)-1646 indicating a reduction of total costs to \$13,045.73 (the Commission's contribution totals \$6,800.00 and that of Duke University is \$6,245.73). The Commission's contribution will be \$5,300.00 in new funds plus the unexpended balance available from the present contract period (1954-1955). Should more than \$1,500.00 be available from the present period, may it be applied to those items which have been reduced or deleted from the budget originally submitted for 1955-1956?

Very truly yours,

Jerome S. Harris
Jerome S. Harris

JSH:ht

cc: Mr. A. S. Brower
Duke University

MAY 20 1955

1110023

E-3198

Administrative Authorization

This revised budget for the renewal of Contract AF-(40-1)-1646 between the United States Atomic Energy Commission and Duke University is hereby approved and authorized.

Jerome S. Harris

Jerome S. Harris, Principal Investigator
Professor of Pediatrics and Associate
Professor of Biochemistry,
Duke University School of Medicine

A. S. Brewer

A. S. Brewer, Business Manager and
Comptroller,
Duke University

5/17/55

Date

A. The Contractor will furnish as its contribution to the project:

1. Salaries of staff members, including the Project Leader, and other personnel engaged in the work in excess of the Government's payment as given below.
2. Use of laboratory space, facilities and equipment, and the furnishing of supplies, in excess of the Government's payment as given below.
3. All clerical, administrative and overhead costs in excess of the Government's payment as given below.

B. Projected Budget.

	Requested of Commission	From other funds administered by Duke University
1. Personnel		
Technician - Mrs. Graham	3600.00	2500.00
Assistant	600.00	1000.00
		500.00
		250.00
		<u>4250.00</u>
Personnel subtotal	<u>4200.00</u>	
2. Equipment		
Count rate meter and Recorder. Shop time	700.00	
3. Supplies		
Isotopes, glassware, animals, illustrations, chemicals	372.46	250.00
4. Travel and communications		
Subtotal	<u>5498.46</u>	<u>4700.00</u>
5. Indirect costs ¹	1527.54	
	<u>6000.00</u>	<u>1545.73</u>
		<u>6245.73</u>

¹ Allocation of indirect costs (including Social Security) is based on 36.37% of salaries and wages; the rate was determined by U. S. Army Audit Agency for year 1953-54 and has been applied to all Army, Air Force, Navy and Ordnance contracts in force at Duke University.

PROJECT FOR 1955-1956.

1. The title of the project will be "Studies of Electrolyte and Fluid Balance in Health and Disease".
2. The work done under this title will continue to be carried out by Duke University in the Departments of Pediatrics and Biochemistry of the School of Medicine.
3. The work will be done as previously under the direction of Dr. Jerome S. Harris, Professor of Pediatrics and Associate Professor of Biochemistry. Curriculum vitae and bibliography have been previously submitted. It is anticipated that 25% of his time will be devoted to this project.

Assisting in certain phases of the project will be:

a) Dr. Will C. Sealy, Associate Professor of Surgery, Duke University School of Medicine and Surgeon-in-charge of the Division of Thoracic Surgery at Duke Hospital. Dr. Sealy is a member of the Society of University Surgeons, American Association for Thoracic Surgery, Southern Society for Clinical Research and has contributed numerous articles to the surgical literature. It is anticipated that 10% of Dr. Sealy's time will be spent on this project.

b) Dr. W. G. Young, Jr., Assistant resident in Surgery at Duke Hospital. Dr. Young graduated from [REDACTED] and served in the United States Navy from 1951-1953. Ten per cent of Dr. Young's work will be devoted to this project.

4. The period of the project will extend from July 1, 1955 to June 30, 1956.
5. Nature and scope of the problem.

The objectives of the proposed project will be:

A. To continue studies of cardiac muscle electrolyte metabolism and its relation to arrhythmia,—particularly that produced by hypercapnia. Three techniques will be used to clarify these relationships.

1. Exposure of the intact animal to varying concentrations of carbon dioxide and measurement of potassium and tissue electrolytes as done previously. In the progress report for last year, it has been noted that potassium is much more toxic to the heart during the hypercapnic state and that high concentrations of carbon dioxide are actually protective. It is planned to alter the acid-base balance of animals by the administration of alkali and acids intravenously (simulating metabolic acid-base disturbances) and at the same time altering the alveolar carbon dioxide content. Theoretically various combinations of intracellular and extracellular pH changes can be so produced. The effect of these changes upon potassium metabolism, toxicity of administered potassium, cardiac electrolyte content, and electrocardiographic tracings will be measured.

2. Studies on the surviving cat heart.

In last year's progress report, mention was made of the use of the surviving cat heart in a Langendorff apparatus which permits rapid changes of environment (perfusing fluid). Studies similar to those done on the intact animal can be performed more rapidly and precisely on the isolated heart. Thus the effect of hypercapnia can be examined by equilibrating the perfusing fluid with high concentrations of carbon dioxide.

This preparation will also be used to measure the rate of uptake of potassium by the heart. $K^{42}Cl$ will be added to the perfusing fluid and the radioactivity measured by beta counting of the perfusing and the effluent from the heart. We have already tried, with satisfactory results, a thin wall jacketed geiger counter coupled to a count rate meter for this purpose. In addition the use of scintillation counters held close to the isolated heart has proved feasible in our hands for measuring the rate of uptake of the radioactive potassium into the cardiac muscle. We plan to use these techniques more fully with the surviving heart under different physiological conditions.

3. The injection of $K^{42}Cl$ into the intact rat under different conditions and the measurement of the specific activity of plasma and tissue potassium, at intervals thereafter. These studies to determine the rate and extent of equilibration of tissue potassium, will be a continuation of those done last month. (See progress report).

- B. Studies of the metabolism of potassium with particular reference to the problem of bound and non-exchangeable potassium. An Attempt will be made to study and demonstrate the existence of compounds containing non-exchangeable potassium by observing the behavior of potassium (labeled with K^{42}) of tissue preparations and compounds obtained therefrom on paper chromatograms and electrophoretic patterns. The possibility of such compounds has been suggested by reports in the literature on non-exchangeable potassium in brain and kidney. Potassium complexes with adenosine triphosphate have actually been demonstrated by Melchior (J. Biochem. 208: 615, 1954). If such complexes are present and can be demonstrated in tissues, a highly significant advance would be made towards our understanding of potassium metabolism.

PROPOSED BUDGET FOR JULY 1, 1955 THROUGH JUNE 30, 1956

A. The Contractor will furnish as its contribution to the project:

1. Salaries of staff members, including the Project Leader, and other personnel engaged in the work in excess of the Government's payment as given below.
2. Use of laboratory space, facilities and equipment, and the furnishing of supplies, in excess of the Government's payment as given below.
3. All clerical, administrative and overhead costs in excess of the Government's payment as given below

B. Projected Budget.

Requested of Commission

From other Funds
administered by Duke University

1. Personnel

Technician - Mrs. Graham
Assistant

Dr. J. S. Harris (part time) 2500.00
Dr. W. C. Sealy (part time) 1000.00
Dr. W. G. Young, Jr. 500.00
Miss Wagner, secretary 250.00

Subtotal 4250.00

Personnel subtotal 4500.00

2. Equipment

Count rate meter and
Recorder; Shop time

750.00

3. Supplies

Isotopes, glassware, animals,
illustrations, chemicals

750.00

250.00

4. Travel and communications

200.00

subtotal 6200.00

200.00

4700.00

	total	6200.00	4700.00
5. Indirect costs ²		<u>1636.65</u>	1545.23
	Total	7836.65	6245.73
6. Estimated Balance from 1954-55 Budget.		1,500.00	

Footnotes.

1. The count rate meter and recorder are to be used in conjunction with the scintillation counter to determine uptake of radioactive potassium by the surviving heart. It will also assist in the location of K42 on the paper chromatograms (see text).
2. Allocation of indirect costs (including Social Security) is based on 36.37% of salaries and wages; the rate was determined by U. S. Army Audit Agency for year 1953-54 and has been applied to all Army, Air Force, Navy and Air Force contracts in force at Duke University.

Administrative Authorization

This application, for renewal of Contract AT-(40-1)-1646 between the United States Atomic Energy Commission and Duke University is hereby approved and authorized.

Jerome S. Harris
Jerome S. Harris, Principal Investigator
Professor of Pediatrics and Associate
Professor of Biochemistry,
Duke University School of Medicine

A. S. Brower
A. S. Brower, Business Manager and
Comptroller,
Duke University

March 31, 1955
Date

Office Memorandum • UNITED STATES GOVERNMENT

TO : J. W. Ould, Jr., Assistant General Counsel

DATE: June 14, 1956

FROM : R. G. Humphries, Acting Director, Contract Division

SUBJECT: REQUEST FOR MODIFICATION OF CONTRACT NO. AT-(40-1)-1646 - DUKE UNIVERSITY

SYMBOL: ACD:ARB

It is requested that you prepare an appropriate modification to the subject contract to extend the term of the contract to June 30, 1957, without additional funds. The modification should include provisions for compliance with AEC Manual Chapter 7510.

A Request for Contract Action, dated June 14, 1956, from the Research and Development Division, asking for the above modification, is enclosed.



R. G. Humphries

Enclosures:

1. Request for Contract Action
2. Resume'
3. Cy Ltr, Harding to Harris, 5/21/56
4. Cy Ltr, LeFevre to Harris, 4/29/55
5. Request for Extension of Contract Term

CC: C. S. Shoup
L. D. MacKay
J. Nicholson, w/cy Encl. 1

1. TO: **J. R. Moore** Chairman Contract Board. From: **Res. & Dev. Division**

It is requested that the Contract Board take the necessary action to process the following described contract action in accordance with the provisions of Bulletin OR-O&M-19:

2. Nature of Action Requested

Selection of New Contractor and Negotiation of Contract.

Modification of Contract

No. **AT-(40-1)-1646**

Contractor: **Duke University**
Durham, North Carolina

Review and approval of Contract, Sub-contract or Purchase Order.

Other (Explain)

Number: _____
Name: _____

3. Nature of Services to be Covered by Contract

Construction

Architect-Engineer

Other

(Explain) **Research**

4. Funding

Amount to be Obligated by this Contract Action \$ **None**

Source of Funds

Approved ORO Financial Plan, _____ Quarter, Fiscal Year 19__

Project No. _____ or, Activity No. _____

Funds to be Obligated: Allotment No. _____ (F.Y. 19__ Funds)

Procurement Directive No. _____ Dated _____

Issuing Office _____

Concurrence in Funding Statement: (signed) _____

Joseph L. Potter
Chief, Budget Branch 6/14/56

5. Project or Activity to be Covered by Contract Action:

Location of Work: _____ Construction Directive No. _____

Estimated Cost of Work to be Covered by this Contract Action \$ _____

Schedule: Date Work to Start _____ Estimated Completion Date _____

Description of Project or Activity:

(If more space is required use separate sheets and attach hereto:)

6. Contract Board Docket
No. _____
(To be assigned by
Board Secretary)

7. Request Submitted By: (signed) _____

JUN 14 1956

Title: _____

C. S. SHOUP
CHIEF BIOLOGY BRANCH
RESEARCH AND DEVELOPMENT DIVISION

8. Complete Description of Services to be Furnished by Contractor:

Washington designated research contract.

Title: "Metabolism and Physiological Role of Potassium and Metabolism of Renal Insufficiency".

(If more space is required use separate sheets and attach hereto:)

9. Description of other changes to be covered by Modification:

Modify contract to extend the period to June 30, 1957, without additional funds. Include provisions for compliance with AEC Manual Chapter 7510.

(If more space is required use separate sheets and attach hereto:)

10. Negotiated Contracts. (Show why it appears desirable to negotiate new contract or to negotiate modification to existing contract)

Letter from C. V. Harding to Dr. Jerome S. Harris, dated May 21, 1956.

(If more space is required use separate sheets and attach hereto:)

11. Contracts, Subcontracts, or Purchase Orders Submitted for Review and Approval: (Furnish brief description of action in this space and attach pertinent documents)

None

12. Disputes:

Attach a statement summarizing the dispute together with pertinent documents and Background Material.

None

1110033

DUKE UNIVERSITY
SCHOOL OF MEDICINE
DURHAM, N. N.

Contract NO. AT-(40-1)-1646

Dr. Jerome S. Harris
Project Leader.

A STUDY OF POTASSIUM METABOLISM IN ISOLATED TISSUE

Resume'

The contractor proposes to continue work until June 30, 1957 utilizing funds already made available under the previous period of performance. The work will include experiments dealing with cardiac arrest in the intact dog circulation, studies of bound and non-exchangeable potassium, of potassium metabolism and acid-base balance, and on the action of changing carbon dioxide in the inspired air and potassium toxicity.

C. S. Shoup

1110034

Office Memorandum • UNITED STATES GOVERNMENT

TO : C. S. Shoup, Chief, Biology Branch
Division of Research and Development, OROO

FROM : Clifford V. Harding, Assistant to Chief, Medical Branch
Division of Biology and Medicine, Washington

SUBJECT: CONTRACT AT(40-1)-1646, JEROME S. HARRIS, DUKE UNIVERSITY

SYMBOL: BMM:CVH

DATE: June 13, 1956

This office approves extension of contract AT(40-1)-1646 to June 30, 1957, without additional appropriation of Atomic Energy Commission funds.

Attachment:
Cpy ltr fr Dr. Harding to
Dr. Harris, dtd 5/21/56

CR MR

F-5254
JUN 1 1956

BMM:CVH

May 21, 1956

Dr. Jerome S. Harris
Department of Pediatrics
Duke University
School of Medicine
Durham, North Carolina

Dear Dr. Harris:

I wish to inform you that the termination date of your contract AT-(40-1)-1646, entitled "I. Metabolism and Physiological Role of Potassium; II. Metabolism of Renal Insufficiency," has been extended to June 30, 1957, without additional appropriation of Atomic Energy Commission funds. You are reminded of Dr. Paul G. LeFevre's letter of April 29, 1955, in which he states that the Contracts Committee does not anticipate further support for this contract.

The Oak Ridge Operations Office will continue to handle the contractual details, and you may expect to hear from a representative of that office shortly with regard to the negotiations.

If we can be of further help, please do not hesitate to write.

Sincerely yours,

Clifford V. Harding
Assistant to Chief
Medical Branch
Division of Biology and Medicine

cc: ✓ Oak Ridge Operations Office

Medical Dep. Dir. Prog. Anal.

Harding:njb
5/18/56

1110036

44-12
MAY 22 1956

BGM: PGL

APP 29 1955

Jerome S. Harris, M. D.
Department of Pediatrics
Duke University
School of Medicine
Durham, North Carolina

Dear Dr. Harris:

Your proposal for another year's renewal of AEC support of the study, "I. Metabolism and Physiological Role of Potassium; II. Metabolism of Renal Insufficiency," has been given general approval by our Contracts Review Committee; it was not possible, however, to make available the full amount requested, and we hope that you will be able to operate satisfactorily with a Commission contribution of \$5,300 (plus the unexpended balance). This renewal will constitute the seventh year of Commission support of this program, and the Committee indicated that further support beyond this next year is not anticipated.

The Oak Ridge Operations Office will continue to handle the contractual details, and you may expect to hear from a representative of that office shortly with regard to the negotiations.

We will, of course, be happy at any time to consider, in competition with other new proposals, the possibility of AEC support of any new studies which you feel would have bearing on our research objectives.

Sincerely yours,

Paul G. LaFevre
Assistant to Chief (Research)
Medical Branch
Division of Biology and Medicine

✓ CC: Oak Ridge Operations Office

Medical

LaFevre:gas

4/28/55

1646

1110037

Request for Extension of Contract Term

It will be noted in the Progress Report for this year that many interesting facets of the work remain to be explored and fully confirmed. Many of these experiments are time consuming and can be done only by a complete team of individuals,— an example in point are those experiments dealing with cardiac arrest in the intact dog whose circulation is being maintained by an artificial pump. In addition, work on some aspects of the project had to be temporarily halted because of the loss of one of the technicians.

For these reasons, an extension of the contract term for another year is requested. There are probably sufficient funds available to complete the main aspects of the proposed research problem since expenditures were not as heavy this year as anticipated and there was a somewhat greater carry over from last year than expected. Until March 1, 1956, approximately \$4,000.00 had been expended and the estimate for the remainder of the original contract period would be \$1,500 —\$2,000. This would leave approximately \$3,500.00 unexpended by the end of the present contract period. For convenience, a copy of last years budget is appended. Additional funds are not requested but permission is requested to extend the present contract term until June 30, 1957.

BUDGET FOR JULY 1, 1955 THROUGH JUNE 30, 1956

	ATC	Contractor	Total
1. Salaries and Wages			
Dr. Jerome S. Harris		2,500.00	2,500.00
Other faculty		1,500.00	1,500.00
Research assistants, technician.	4500		4,500.00
Secretarial assistance		250.00	250.00
Subtotal	<u>4,500.00</u>	<u>4,250.00</u>	<u>8,750.00</u>
2. Equipment	750.00		750.00
3. Supplies	750.00	250.00	1000.00
4. Travel and Communications	163.36	200.00	363.36
5. Indirect costs *	<u>1,636.64</u>	<u>1,545.73</u>	<u>3,182.37</u>
	7,800.00	6,245.73	14,045.73

* Allocation of indirect costs (including Social Security) is based on 36.37% of salaries and wages; the rate was determined by U. S. Army Agency for year 1953-54 and has been applied to all Army, Air Force, Navy and Ordnance contracts in force at Duke University.

Administrative Authorization

This application, for extension of the term of Contract AT-(40-1)-1646 between the United States Atomic Energy Commission and Duke University is hereby approved and authorized.

Jerome S. Harris
Jerome S. Harris, Principal Investigator
Professor of Pediatrics and Associate
Professor of Biochemistry,
Duke University School of Medicine

A. S. Brower
A. S. Brower, Business Manager and
Treasurer,
Duke University

March 31, 1956
Date

April 24, 1956

C. S. Shoup
Chief, Biology Branch
Research and Development Division
United States Atomic Energy Commission
Oak Ridge, Tennessee

Re: ORS:EMM

Subject: Contract No. AT-(40-1)-1646

Dear Doctor Shoup:

I am enclosing the information you requested in your letter of April 11, 1956. You will note the total expenditure projected for the period of the extension of the contract term is one half of the 1955-1956 budget. Of this sum, the contractors portion is \$3,122.87,- which will be furnished from new funds by the contractor. Of the total, the Atomic Energy Commission's portion is \$3,900.00. This amount will be available from the unexpended balance so that new funds are not requested from the Atomic Energy Commission.

I trust that this will clear up the matter and that permission will be granted to extend the Contract term under the above provisions which do not require new monies from the Atomic Energy Commission.

Sincerely yours,


Jerome S. Harris, M. D.
Principal Investigator
Professor of Pediatrics
Associate Professor of Biochemistry
Duke University School of Medicine
Durham, North Carolina

Approved:


A. S. Brower, Business Manager
and Treasurer
Duke University
Durham, North Carolina

1110041

F-3412

Estimated Expenditures 1955 - 1956

	AFC	Contractor	Total
To March 1956	4,000.00	4163.82	8163.82
To June 30, 1956	1,900.00	2081.91	4081.91
Total	6,000.00	6245.73	12245.73
Unexpended Balance	1,900.00		1900.00
Total carry-over*	3,900.00		3900.00

* Includes previous unexpended balance.

Anticipated Utilization of Funds for the Proposed Extended Period

In general, all personnel will give only approximately one half the time previously requested. Thus a part-time technician will be employed instead of a full time technician. All other expenditures have been similarly reduced.

	AFC ¹	Contractor ²	Total
1. Salaries and Wages			
Dr. Jerome S. Harris		1,250.00	1,250.00
Other faculty		750.00	750.00
Research assistant and Technician	2,250.00		2,250.00
Secretarial Assistance		125.00	125.00
Subtotal	2,250.00	2,125.00	4,375.00
2. Equipment & Supplies	750.00	125.00	875.00
3. Travel & Communications	144.32	64.73	109.05
4. Indirect Costs ³	855.68	808.14	1,663.82
5. Total	3,900.00	3,122.87	7,022.87

* 38.03% of salaries and wages.

Footnotes.

1. AFC funds from anticipated unexpended balance.
2. New funds from contractor.
3. 38.03% of salaries and wages.

F-3412

APR 27 1956

Incident Report

No serious incidents, industrial losses (from fires, explosions, lightning, windstorms, floods or sprinkler leakage), other property damage, accidents or personal injuries have occurred in connection with work performed under Contract AT-(40-1)-1646 between the United States Atomic Energy Commission and Duke University.

Jerome S. Harris

Jerome S. Harris, Principal Investigator
Professor of Pediatrics and Associate
Professor of Biochemistry,
Duke University School of Medicine

April 24, 1956.

Date

In Reply Refer To:
ADC:JN

Oak Ridge, Tennessee
June 13, 1955

Duke University
Department of Pediatrics
Durham, North Carolina

Attention: Dr. J. S. Harris

Subject: MODIFICATION NO. 2 TO CONTRACT NO. AT-(40-1)-1646

Gentlemen:

Enclosed, duly signed on behalf of the Commission, are three copies of Modification No. 2 to the subject contract which provides the program and budget for the third period of performance beginning July 1, 1955 and ending June 30, 1956. Also enclosed is a Notice of Research Project form which is to be used insubmitting your summary statement.

If the modification, as submitted, is satisfactory to you it is requested that you sign the copies thereof in the space provided for the Senior Investigator and have the copies signed by the proper official of the University, returning one copy to this office. The two remaining copies are for your retention. The summary statement should be returned along with the signed copy of the modification prior to June 30, 1955.

Very truly yours,

ORIGINAL SIGNED BY JOHN E. MOORE

John E. Moore
Director, Contract Division
Oak Ridge Operations

✓
Enclosures:
Mod. 2 (in trip.)
Notice of Res. Project Form 1:22

Nicholson:jn

OAK RIDGE OPERATIONS

AIR MAIL

CONTRACT COORDINATION BRANCH	CONTRACT DIVISION	DISPATCHED			
OFFICE ▶					
SURNAME ▶	Nicholson	Moore			
DATE ▶	6-13-55	JUN 15 1955			

98-5.31

In Reply
Refer to: OR:ER

Oak Ridge, Tennessee
May 26, 1955

Dr. J. S. Harris
Department of Pediatrics
Duke University
Durham, North Carolina

Subject: CONTRACT NO. AT-(40-1)-1646

Dear Dr. Harris:

We have initiated action for the preparation of a modification to Contract No. AT-(40-1)-1646 to extend the period to June 30, 1956, with the Commission contributing \$5,300 in new funds to the total cost of \$14,045.73. A copy of the budget to be included in the modification is enclosed for your information. The modification will be mailed to you for signature as soon as it is complete. We shall appreciate your prompt attention to the modification when you receive it so we may receive our copies back as soon as possible.

You will note that the enclosed budget does not agree with the revised budget as submitted by your letter of May 17, 1955. In our letter of May 4, 1955, we inadvertently listed \$1,500 as being available from the previous period instead of the \$2,500 as pointed out in your letters of April 18 and May 5, 1955. Therefore, we recomputed the budget to include the extra \$1,000. In the event additional funds remain unexpended on June 30, they may be used under the contract.

Your cooperation in this matter is appreciated.

Very truly yours,

ORIGINAL SIGNED BY
HERMAN M. ROTH

Herman M. Roth
Director
Research and Medicine Division

Enclosure:
Budget

CC: A. S. Brower, North Carolina
J. R. Moore

Rooseville:lr

15204

1110045

Mod. 1 to Cont. AT-(40-1)-1646

Duke University

Distributed June 28, 1954

Washington
Contract files (2)
Finance (2)
Research & Medicine (2)
Washington (B&M-2)
extra copies

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Duke University
DURHAM
NORTH CAROLINA

School of Medicine
Department of Pediatrics
Reply to Undersigned

June 22, 1954

Dr. R. G. Humphries, Acting Director
Contract Division
Oak Ridge Operations
United States Atomic Energy Commission
Oak Ridge, Tennessee

Dear Dr. Humphries:

Re: ADC:JN

I am enclosing a signed copy of the Supplemental Agreement modifying contract No. AT-(40-1)-1646.

Sincerely yours,



Jerome S. Harris, M. D.

JSH:ljm

c/c Mr. G. C. Henricksen
Duke University

1110048

In Reply Refer To:
ADC:JN

Oak Ridge, Tennessee
June 18, 1954

Duke University
Department of Pediatrics and Biochemistry
Durham, North Carolina

Attention: Dr. Jerome S. Harris

Subject: MODIFICATION NO. 1 TO CONTRACT NO. AT-(40-1)-1646

Gentlemen:

Enclosed, duly signed on behalf of the Commission, are three copies of the subject modification which provides the program and budget for the second period of performance beginning July 1, 1954 and ending June 30, 1955.

If the modification, as submitted, is satisfactory to you it is requested that you sign the three copies thereof in the space provided for the Senior Investigator and have the copies signed by the proper official of the University, returning one signed copy to this office. The two remaining copies are for your retention.

Very truly yours,

R. G. Humphries
Acting Director
Contract Division
Oak Ridge Operations

RGH
Enclosure:
Mod. 1 (in trip.)

Nicholson:jn

b400111

CONTRACT COORDINATION BRANCH	
OFFICE ▶	<i>Acting Director</i> <i>Contract Division</i>
SURNAME ▶	<i>Nicholson</i> <i>Humphries</i>
DATE ▶	<i>6-18-54</i> <i>6-18-54</i>

Duke University
DURHAM
NORTH CAROLINA

School of Medicine
Department of Pediatrics
Reply to Undersigned

4 August 1953

Dr. John R. Moore, Director
Contract Division
Oak Ridge Operations
U. S. Atomic Energy Commission
Oak Ridge, Tennessee

Dear Dr. Moore:

I am enclosing the two hundred word summary on
Scope and Purpose of Contract No. AT-(40-1)-1646,
which you requested in your letter of June 29, 1953.

I am very sorry that through a misunderstanding
this was not sent to you sooner. I hope that you will
forgive the delay.

Sincerely yours,

Jerome S. Harris
Jerome S. Harris

JSH:ht
Encl.

1110050

C-4030

SUMMARY OF SCOPE AND PURPOSE OF CONTRACT NO. AT-(40-1)-1646

The objectives of this work will be: (a) to continue studies of electrolyte and fluid balance in health and disease and (b) to study the metabolism of renal insufficiency, with particular reference to iron and anemia.

The first objective is a continuation of the general program which has been approached through investigations of potassium metabolism in isolated tissues. It is now proposed to use radioactive potassium to study the equilibrium between surviving tissue slices and their environment. The rates of uptake and discharge of this substance from surviving tissues will be measured and the influence of various conditions on these rates will be determined. From these data, the problem of the existence of bound or non-exchangeable potassium may be resolved.

The second objective emerged from clinical observations and work done last year on the metabolism of nephrectomized dogs. It was noted that nephrectomized dogs showed a striking and rapidly developing anemia which did not respond to ordinary therapy. Preliminary observations showed markedly deficient red blood cell formation (as determined by study of radioactive iron uptake) and also increased destruction (by clinical observations on rate of development of anemia). It is proposed to expand these studies by following the plasma disappearance curves of injected radioactive iron, the uptake of radioiron into red cells, and the rate of disappearance of cells (labelled with radioactive iron) from the circulation in the hope, ultimately, of gaining some insight into the relationship between uremia and anemia.

SUMMARY OF SCOPE AND PURPOSE OF CONTRACT NO. AT-(40-1)-1646

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Contract AT-(110-1)-1646

Duke University

Distributed July 8, 1953

Washington

Contract files (2)

Finance (2)

Research & Medicine (2)

Washington (B&M-2)

extra copies

1110053

DC:JH

Oak Ridge, Tennessee
June 29, 1953

Duke University
Department of Biochemistry
Box 3711
Durham, North Carolina

Attention: Dr. J. S. Harris

Subject: CONTRACT NO. AT-(40-1)-1646

Gentlemen:

Your research project which was submitted to the Commission's Division of Biology and Medicine, Washington, D. C., has been approved by that office in the amount of \$5,681.00 and has been forwarded to this office for preparation of an appropriate contract covering the Commission's support of your project.

Enclosed, duly executed on behalf of the Commission, is a contract numbered as shown in the subject line above, which incorporates in Appendix "A" a description of your project and the budget for the first period which you are to follow as a general guide.

It is requested that you sign each copy of the contract in the space provided for the Project Leader and have the contract signed by the proper official of the University, returning the original to this office. The two remaining copies are for your files.

It will be noted that the contract provides for payment in Article III of a lump sum in consideration of your performance of the research activities described in Appendix "A". The first payment, representing one-half the amount of the agreed compensation, will be paid to you upon your submission of a properly certified voucher on or before the first date established in Article II of the contract. The remaining 50% of the agreed compensation will be paid to you within six months from the date of the first payment.

Performance of a cost audit of your expenditures has been eliminated through this lump sum payment for your research services. It is believed that this will save you considerable time and trouble in detailing your expenditures on cost reimbursement vouchers.

1110054

June 29, 1953

In order to assist you in preparing an appropriate voucher there is enclosed an instruction sheet containing numbered instructions corresponding with numbers appearing on a specimen copy of the voucher form. Vouchers should be submitted to the Oak Ridge Operations office in one original (white) and four copies (yellow) addressed as shown in Article IV of the contract. It is assumed that you will give your business office the benefit of these instructions.

Your attention is called to the reporting requirements outlined in Appendix "G" to the contract, especially to Item No. 2 requiring the immediate submission of a 200 word summary statement describing the purpose and scope of your project.

For your information and guidance in purchasing isotopes through the Commission, in accordance with the provisions of Article VII, there is enclosed a copy of the latest Procurement Procedure for Radioisotopes, together with a set of application forms, which you will use in making purchases of isotopes.

Your particular attention is invited to Appendix "B", Section 12 - Fellowships.

It is believed that the remaining portions of the contract are self-explanatory, however, if you have any questions concerning the application or interpretation of any of the contract provisions I will be glad to furnish you with additional information.

Very truly yours,

John R. Moore
Director
Contract Division
Oak Ridge Operations

JRM
Enclosures:
Contract (in trip.)
Vouchers & Instr. Sheets
Procurement Procedures & Application forms

Nicholson: jn

1110055

OFFICE ▶	Contract				
SURNAME ▶	Nicholson	Turn			
DATE ▶	6-29-53	6-29			

Office Memorandum • UNITED STATES GOVERNMENT

TO : J. W. Ould, Jr., Assistant General Counsel

DATE: May 26, 1954

FROM : R. G. Humphries, Acting Director, Contract Division

SUBJECT: RENEWAL OF CONTRACT NO. AT-(40-1)-1646 - DUKE UNIVERSITY

SYMBOL: ADA:ARB

Enclosed is an approved proposal for renewal of subject contract for a period of one year beginning July 1, 1954. This approval action is covered by Procurement Directive No. BM-54-290, dated May 14, 1954, in the amount of \$6,200.00.

Please prepare an appropriate modification to renew the contract for a period of one year, beginning July 1, 1954, and provide for the payment of \$6,200.00.



R. G. Humphries

Enclosures:

1. Request for Contract Action
2. Budget for Contract AT-(40-1)-1646
3. Resume
4. Memo fm LeFevre dtd 5/14/54
5. Application for Renewal

CC: C. S. Shoup
 L. D. Mackay
 Ed Ziegler, w/Encls. 1, 2 & 3
 J. Nicholson

Brown:arb

RECEIVED
 CONTRACT DIVISION
 MAY 28 1954

1. TO: **J. R. Moore** Chairman Contract Board. From: **Res. & Medicine Division**

It is requested that the Contract Board take the necessary action to process the following described contract action in accordance with the provisions of Bulletin OR-O&M-19:

*OK
H
5/76*

2. Nature of Action Requested

Selection of New Contractor and Negotiation of Contract.

Modification of Contract
No. AT-(40-1)-1646
Contractor: Duke University
Durham, North Carolina

Review and approval of Contract, Sub-contract or Purchase Order.
Number: _____
Name: _____

Other (Explain) _____

3. Nature of Services to be Covered by Contract

Construction Architect-Engineer Other (Explain) **Research**

4. Funding

Amount to be Obligated by this Contract Action \$ 6,200.00

Source of Funds

Approved ORO Financial Plan, _____ Quarter, Fiscal Year 19____
Project No. _____ or, Activity No. _____
Funds to be Obligated: Allotment No. _____ (F.Y. 19____ Funds)
Procurement Directive No. BM-54-290 Dated 5-14-54
Issuing Office Division of Biology and Medicine, Washington

Concurrence in Funding Statement: (signed) _____
Chief, Budget Branch

5. Project or Activity to be Covered by Contract Action:

Location of Work: _____ Construction Directive No. _____
Estimated Cost of Work to be Covered by this Contract Action \$ _____
Schedule: Date Work to Start _____ Estimated Completion Date _____
Description of Project or Activity:

(If more space is required use separate sheets and attach hereto:)

*Procurement Directive
No. BM-54-290, 5/14/54,
\$6,200.00.*

10030

<p>6. Contract Board Docket No. _____ (To be assigned by Board Secretary)</p>	<p>7. Request Submitted By: (signed) <i>Galileo McColey</i> Date: <i>5-26-54</i> Title: <i>Kasschau</i> RESEARCH AND MEDICINE DIVISION</p>
<p>8. <u>Complete Description of Services to be Furnished by Contractor:</u></p> <p>Washington designated research contract.</p> <p>Title: "a. Metabolism and Physiological Role of Potassium b. Metabolism of Renal Insufficiency" (If more space is required use separate sheets and attach hereto:)</p>	
<p>9. <u>Description of other changes to be covered by Modification:</u></p> <p>Renew contract for a period of one year beginning July 1, 1954, with new funds in the amount of \$6,200.00</p> <p>(If more space is required use separate sheets and attach hereto:)</p>	
<p>10. <u>Negotiated Contracts.</u> (Show why it appears desirable to negotiate new contract or to negotiate modification to existing contract)</p> <p>Memo - F. G. LeFevre to K. Kasschau, dated May 14, 1954</p> <p>(If more space is required use separate sheets and attach hereto:)</p>	
<p>11. <u>Contracts, Subcontracts, or Purchase Orders Submitted for Review and Approval:</u> (Furnish brief description of action in this space and attach pertinent documents)</p> <p style="text-align: center;">None</p>	
<p>12. <u>Disputes:</u> Attach a statement summarizing the dispute together with pertinent documents and Background Material.</p> <p style="text-align: center;">None</p>	

Budget for Contract No. AT-(40-1)-1646
For Period July 1, 1954 - June 30, 1955

Salaries and wages:		\$8750.00
Dr. J. S. Harris (Part Time)	\$2500.00	
Other faculty	1500.00	
Research Assistant and Technician	4500.00	
Secretary	2500.00	
Equipment:		1500.00
Supplies:		1000.00
Travel and Communications:		400.00
Indirect Costs:		3171.88
		<hr/>
		\$14,821.88

The Commission's contribution to the above budget will be \$6,950, including \$6,200 in new funds and the unexpended balance of \$750 from the previous period.

RESUME

Studies of electrolyte metabolism will be continued. Further investigations will be made to clarify the relation between potassium metabolism, acute respiratory acidosis and cardiac arrhythmias. The use of radiopotassium may assist in these experiments.

Toxic factors in the etiology of the anemia of renal insufficiency will be investigated. Previous work has revealed a very marked disturbance in the incorporation of radioactive iron into hemoglobin and suggested the presence of a toxic substances which interfere with hemoglobin. A search for the toxic materials will be made in the serum of the nephrectomized dog and perhaps in normal urine and splenic extracts.

UNITED STATES ATOMIC ENERGY COMMISSION

DIVISION OF BIOLOGY AND MEDICINE

WASHINGTON, D. C.

DATE:

TO : Kenneth Kasschau, Director, Research and Medicine Division
FROM : Cak Edge
P. G. LeFevre, Assistant to Chief (Research), Medical Branch
SUBJECT: TRANSMITTAL OF RESEARCH PROPOSAL FOR CONTRACT NEGOTIATION
SYMBOL : BBI:PGL

Les

This letter with enclosure, in triplicate, is sent in accordance with the procedure described in a letter from the General Manager to all Managers of Operations dated January 27, 1949.

1. Institution: Duke University
2. Investigator (s): Jerome S. Harris, M. D.
3. Title: "a. Metabolism and Physiological Role of Potassium"
"b. Metabolism of Renal Insufficiency"
4. () New Contract or (x) Renewal of Contract No. AT(40-1)1646
5. Duration - From: July 1, 1954 to June 30, 1955
6. AEC Technical Supervision: Medical Branch
7. Recommended Support: \$6,200.00 (\$6,950.00 less unexpended balance of \$750.00)
Authorized by Procurement Directive No. BM54-290
Issued _____ \$ 6,200.00
Activity No. 6300
8. Other Comments:

Please note change in title.

Title to equipment purchased under the terms of this contract should be vested in the University.

8. Comments (Continued)

9. Security Requirements:

In accordance with the provisions of GM-93 (Revised March, 1950), and the requirements of the Declassification Guide, the Division of Biology and Medicine has determined that the following security precautions should be taken in connection with the proposed research contract.

Since there is essentially zero chance that restricted data will be required or developed, no personnel security requirements should be imposed.

10. Reports: Reports are to be required as provided for by Memorandum Instruction of November 9, 1949, on subject "Direct Research Contract Reports".

() Special Reports Instructions are as follows:

- Enclosures:
- () "A" - Proposal, dated Sent to OROC by investigator
 - () "B" - Notification letter, dated _____
 - () "C" - Other correspondence, _____ letters
 - "D" - Procurement Directive BMSI-290

Distribution:

- | | |
|---|--|
| <p>Addressee: Original (w encl.)
1st Copy (w encl.)
2nd Copy (w encl.)</p> <p>Program Analysis
Branch: White Copy (w/o encl.)</p> | <p>Division File: Yellow Copy (w encl.)
Pink Copy (w/o encl.)</p> <p>Branch File: White Copy (w encl.)</p> |
|---|--|

UNITED STATES ATOMIC ENERGY COMMISSION
DIVISION OF BIOLOGY AND MEDICINE
WASHINGTON, D. C.

DATE:

TO : Kenneth Kasschau, Director, Research and Medicine Division
Oak Ridge
FROM : P. G. LaFevre, Assistant to Chief (Research), Medical Branch
SUBJECT: TRANSMITTAL OF RESEARCH PROPOSAL FOR CONTRACT NEGOTIATION
SYMBOL : EMM:FGL

This letter with enclosure, in triplicate, is sent in accordance with the procedure described in a letter from the General Manager to all Managers of Operations dated January 27, 1949.

1. Institution: Duke University
2. Investigator (s): Jerome S. Harris, M. D.
3. Title: "a. Metabolism and Physiological Role of Potassium"
"b. Metabolism of Renal Insufficiency"
4. () New Contract or () Renewal of Contract No. AT(40-1)1646
5. Duration - From: July 1, 1954 to June 30, 1955
6. AEC Technical Supervision: Medical Branch
7. Recommended Support: \$6,200.00 (\$6,950.00 less unexpended balance of
750.00) EM54-290
Authorized by Procurement Directive No. _____
Issued _____ \$ 6,200.00
Activity No. 6300
8. Other Comments:

Please note change in title.

Title to equipment purchased under the terms of this contract should be vested in the University.

1110063

8. Comments (Continued)

9. Security Requirements:

In accordance with the provisions of GM-93 (Revised March, 1950), and the requirements of the Declassification Guide, the Division of Biology and Medicine has determined that the following security precautions should be taken in connection with the proposed research contract.

Since there is essentially zero chance that restricted data will be required or developed, no personnel security requirements should be imposed.

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() Special Reports Instructions are as follows:

Enclosures: () "A" - Proposal, dated Sent to OROC by investigator
() "B" - Notification letter, dated _____
() "C" - Other correspondence, _____ letters
 () "D" - Procurement Directive BM54-290

Distribution:

Addressee: Original (w encl.) Division File: Yellow Copy (w encl.)
 1st Copy (" ") Pink Copy (w/o encl.)
 2nd Copy (" ") Green Copy (" ")
Program Analysis Branch File: White Copy (w ")
Branch: White Copy (w/o encl.)

Application for Renewal
of
Contract No. AT-(40-1)-1646

between

Duke University

and

U. S. Atomic Energy Commission

75
1110065

March, 1954

Duke University School of Medicine

PROGRESS REPORT

Work done under Contract No. AT- (40-1)-1646

between

Duke University and the United States Atomic Energy Commission

under the direction of Dr. Jerome S. Harris.

1. Studies of Electrolyte and Fluid Balance in Health and Disease.

The first objective of this year's project was to study the equilibrium between surviving tissues and their environment through the use of radioactive potassium. The rates of uptake and discharge of this substance from surviving tissues were to have been measured. However, while preliminary studies were in progress, a series of papers by Mudge and his co-workers appeared on this subject. (Am. J. Physiol. 173: 511, 1953 and Proc. Soc. Exp. Biol. and Med. 82: 675, 1953). Mudge measured the rate of uptake of radioactive potassium by surviving rabbit kidney slices and found intracellular potassium to be non-homogeneous. There was a non-exchangeable (bound) potassium during the anaerobic state which became freely exchangeable with the potassium of the suspending medium during aerobiosis. Mudge was able to locate part of this non-exchangeable potassium in the mitochondria.

Because of these reports, which accomplished some of the proposed objectives of this grant, our attention was directed towards the possible importance of potassium in studies on cardiac arrest which had been under investigation concurrently with Drs. Sealy and Young of the Department of Surgery at Duke Medical School. Preliminary results were so promising that most of the year's work (with the exception of the studies on the anemia of nephrectomized dogs as described below) was devoted to this aspect of potassium metabolism.

Acute cardiac arrest or fibrillation is one of the most serious catastrophes which may occur during surgery. With the increasing length and intricacy of present day surgical procedures, the incidence of cardiac standstill has increased and it is now a major threat to the welfare of the patient during operations. Our previous studies had implicated acute respiratory acidosis (hypercapnia) as an important factor in the etiology of the condition. During the course of these studies, we were struck by the resemblance of the electrocardiographic changes during hypercapnia to those occurring in potassium intoxication. The relationship of acute respiratory acidosis to potassium metabolism was therefore studied. It was found that acute prolonged hypercapnia caused a marked rise in plasma potassium in both dog and rat and that there was a further rise in potassium concentration during the immediate post-hypercapnic period. These observations were correlated with electrocardiographic manifestations which tended to parallel

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the serum potassium levels and were also more marked during the post-hypercapnic period when arrest and fibrillation are more likely to occur. Analysis of rat tissues for water and electrolytes showed interesting changes in the heart during hypercapnia. Further study of these changes is contemplated.

The work has been summarized in two abstracts which are appended. The first "Electrolyte Metabolism and Cardiac Arrhythmias during Acute Prolonged Hypercapnia" was given before the Southern Society for Clinical Research on January 30, 1954 and the second "The Role of Intracellular and Extracellular Electrolytes in the Cardiac Arrhythmias Produced by Prolonged Hypercapnia" was presented to the Society of University Surgeons on February 13, 1954. This paper has been accepted for publication by "Surgery". (appended)

2. The Metabolism of Renal Insufficiency with particular reference to iron anemia.

As explained in last year's progress report and project outline, nephrectomized dogs maintained by intermittent peritoneal lavage rapidly develop a very severe anemia, which responds only to transfusions. This anemia resembles that seen in clinical states of renal insufficiency and provide an opportunity to investigate the problem. Our objective of determining the mechanism of this anemia through the use of radioactive iron has largely been accomplished. The work is summarized in a report (appended) which is to be given before the American Society of Biological Chemists in April, 1954 and is being prepared for formal publication. Briefly, the anemia was found to be due to an almost complete cessation of hematopoiesis together with a shorter life span of both native and transfused red cells. Attempts to restore hematopoiesis in presence of the renal insufficiency were fruitless. The results indicate that there is a toxic suppression of the bone marrow and suggest the possibility of searching for the toxic agent with the aid of an assay method involving the uptake of radioactive iron by nucleated or reticulated red cells in vitro.

PROJECT FOR 1954-1955.

1. The title of the Project will be Studies of Electrolyte and Fluid Balance in Health and Disease.
2. The work done under this title will continue to be carried out by Duke University (Department of Pediatrics and Biochemistry) under the direction of Dr. Jerome S. Harris, Professor of Pediatrics and Associate Professor of Biochemistry. Curriculum vitae and bibliography have been previously submitted. It is anticipated that 25% of his time will be devoted to this project.

Assisting in certain phases of the project will be:

- a) Dr. Will C. Sealy, Associate Professor of Surgery, Duke University School of Medicine and Surgeon-in-charge of the Division of Thoracic Surgery at Duke Hospital. Dr. Sealy is a member of the Society of University Surgeons, American Association for Thoracic Surgery, Southern Society for Clinical Research and has contributed numerous articles to the surgical literature. It is anticipated that 10% of Dr. Sealy's time will be spent on this project.
- b) Dr. W. G. Young, Jr., Assistant resident in Surgery at Duke Hospital. Dr. Young graduated from [REDACTED] and served in the United States Navy from 1951-1953. Ten percent of Dr. Young's work will be devoted to this project.

3. The period of the project will extend from July 1, 1954 to June 30, 1955.
4. Nature and Scope of the Problem.

The objectives of the proposed project will be:

- a) To continue the studies of electrolyte metabolism and
- b) To investigate toxic factors in the etiology of the anemia of renal insufficiency.

a. The first objective is a continuation of previous studies summarized in this year's annual report. Further investigations will be made to clarify the relation between potassium metabolism, acute respiratory acidosis and cardiac arrhythmias. These studies will include analysis of cardiac muscle at different intervals during and after hypercapnia, attempts to alter the hyperpotassemia and arrhythmias of acute hypercapnia by such agents as glucose, saline, adrenolytic agents and low potassium diets, determinations of the effect of hypercapnia on the toxicity of potassium and the influence of cardiac glycosides upon both hyperpotassemia and electrocardiographic phenomena. The use of radiopotassium may assist in the solution of these problems. Determination of uptake of radiopotassium by the heart under the conditions mentioned above would perhaps furnish a more dynamic picture of the events than the analyses for potassium content alone. Further several other pathways for investigation of these phenomena may be explored. Results by other investigators have shown the presence of non-exchangeable potassium in kidney and in adult brain. Similar studies have not been done on the heart and determination of the state of potassium with radioactive potassium under normal activity, hypercapnia and drugs would appear indicated.

b. The second objective is to investigate the etiology of the disturbance of hemoglobin metabolism in renal failure. As mentioned in the progress report for last year, a severe anemia develops in the nephrectomized dog (maintained on intermittent peritoneal lavage) which resembles that seen in human renal insufficiency. Our studies have shown a very marked disturbance in the incorporation of radioactive iron into hemoglobin in the former condition and suggested the presence of toxic substances which interfere with hemoglobin metabolism. It is proposed that a search be made for this toxic material in the serum of the nephrectomized dog using the in vitro incorporation of radioactive iron into nucleated (avian) or mammalian reticulated erythrocytes as the assay method. Source materials for other possible depressant substances would be normal urine and splenic extracts - since the spleen has been thought to produce substances which inhibit red blood cell formation in several clinical states.

PROPOSED BUDGET FOR JULY 1, 1954 THROUGH JUNE 30, 1955

a) The Contractor will furnish as its contribution to the project:

1. Salaries of staff members, including the Project Leader, and other personnel engaged in the work in excess of the Government's payment as given below.
2. Use of laboratory space, facilities and equipment, and the furnishing of supplies, in excess of the Government's payment as given below.
3. All clerical, administrative and overhead costs in excess of the Government's payment as given below

b) Projected Budget.

	Requested of Commission	From other Funds administered by Duke University
1. Personnel		1. Personnel
Technician - Mrs. Dillon	3600.00	Dr. J. S. Harris (part time) 2500.00
Assistant	900.00	Dr. W. C. Sealy (part time) 1000.00
	<u> </u>	Dr. W. G. Young, Jr. 500.00
	4500.00	Mrs. McKee, secretary <u>250.00</u>
Personnel subtotal	4500.00	subtotal 4250.00
2. Equipment		2. Equipment
Scintillation Counter and Shield	750.00	Electrocardiograph 750.00
3. Supplies	750.00	3. Supplies 250.00
isotopes, glassware, animals, illustrations, chemicals.		
4. Travel and communications	<u>200.00</u>	4. Travel <u>200.00</u>
subtotal	6200.00	subtotal 5450.00

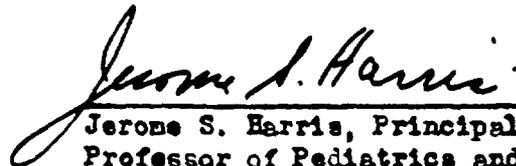
5. Indirect costs ²	subtotal	6200.00	subtotal	5450.00
		<u>1631.25</u>		<u>1540.63</u>
6. Estimated Balance from 1953-54 Budget.	Total	7831.25	Total	6990.63
		750.00		

Footnotes.

1. The scintillation counter is needed to count Po²¹⁰ accurately and to simplify the counting of tissue activity and to enable the technicians to work with smaller magnitude of radioactivity.
2. Allocation of Indirect costs is based on 36.25% of salaries and wages; the rate was determined by U. S. Army Audit Agency for year 1952-53 and has been applied to all Army, Air Force, Navy and Ordnance contracts in force at Duke University.

Administrative Authorization

This application, for renewal of Contract AT-(40-1)-1646 between the United States Atomic Energy Commission and Duke University is hereby approved and authorized.



Jerome S. Harris, Principal Investigator
Professor of Pediatrics and Associate
Professor of Biochemistry,
Duke University School of Medicine



G. C. Henricksen, Assistant Business
Manager and Comptroller,
Duke University

3/30/54
Date

Office Memorandum • UNITED STATES GOVERNMENT

TO : J. W. Child, Jr., Assistant General Counsel

DATE: June 15, 1953

FROM : John R. Moore, Director, Contract Division

SUBJECT: REQUEST FOR PREPARATION OF A LUMP-SUM RESEARCH CONTRACT WITH
DUKE UNIVERSITY, DR. J. S. HARRIS, PROJECT LEADER.

SYMBOL: AD:ARB

Enclosed is a proposal from Duke University, which has been approved by the Division of Biology and Medicine, for a research project entitled "A Study of Potassium Metabolism in Isolated Tissue", with Dr. J. S. Harris as Project Leader. This approval is covered by Procurement Directive No. BM-53-293, in the amount of \$19,386.00.

This work will be the continuation of the research work started under Title III of Contract No. AT-(40-1)-289.

It is requested that you prepare a new lump-sum type contract to cover this program in the amount of \$5,501.00, including overhead at 8%, for a period of one year beginning July 1, 1953.


John R. Moore

Enclosures:

1. Request for Contract Action
2. Budget
3. Resume
4. Memo fm LeFevre dtd 5/26/53
5. Cy Ltr fm Handler dtd 5/7/53
6. Cy Ltr fm LeFevre dtd 5/20/53
7. Progress Report and Proposal

CC: C. S. Shoup
L. D. MacKay
Ed Ziegler, w/Encl. 1
J. Nicholson

/arb

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4-2-53

1. **John R. Moore, Director** Chairman
TO: **Contract Division** Contract Board. From: Research & Medicine Division

It is requested that the Contract Board take the necessary action to process the following described contract action in accordance with the provisions of Bulletin OR-O&M-19:

2. Nature of Action Requested

- Selection of New Contractor and Negotiation of Contract.
Duke University
Durham, North Carolina
- Modification of Contract
No. _____
Contractor: _____
- Review and approval of Contract, Sub-contract or Purchase Order.
Number: _____
Name: _____
- Other (Explain) _____

3. Nature of Services to be Covered by Contract

Construction Architect-Engineer Other (Explain) **Research**

4. Funding

Amount to be Obligated by this Contract Action \$ **5,681.00**

Source of Funds

Approved ORO Financial Plan, _____ Quarter, Fiscal Year 19____
Project No. _____ or, Activity No. _____
Funds to be Obligated: Allotment No. _____ (F.Y. **5/26/53** Funds)
Procurement Directive No. **BA-53-293** Dated _____
Issuing Office **Div. of Biology and Medicine, Washington**

Concurrence in Funding Statement: (signed) _____
Chief, Budget Branch

5. Project or Activity to be Covered by Contract Action:

Location of Work: _____ Construction Directive No. _____
Estimated Cost of Work to be Covered by this Contract Action \$ _____
Schedule: Date Work to Start _____ Estimated Completion Date _____
Description of Project or Activity:

(If more space is required use separate sheets and attach hereto:)

*Procurement Directive
No. BM-53-293, 5/26/53
\$19,386.00.*

<p>6. <u>Contract Board Docket</u> No. _____ (To be assigned by Board Secretary)</p>	<p style="text-align: right;">Original signed by _____</p> <p>7. Request Submitted By: (signed) _____ Date: _____ Assistant Director RESEARCH AND MEDICINE DIVISION Acting Assistant Director Research and Medicine Division</p>
<p>8. <u>Complete Description of Services to be Furnished by Contractor:</u></p> <p>Washington Designated Research Contract</p> <p>Title: (a) A Study of Potassium Metabolism in Isolated Tissue</p> <p style="text-align: center;">(If more space is required use separate sheets and attach hereto:)</p>	
<p>9. <u>Description of other changes to be covered by Modification:</u></p> <p>New contract for a period of one year, beginning July 1, 1953. The work under this contract will be the continuation of the research work started under Title III, Contract No. AT-(40-1)-269.</p> <p style="text-align: center;">(If more space is required use separate sheets and attach hereto:)</p>	
<p>10. <u>Negotiated Contracts.</u> (Show why it appears desirable to negotiate new contract or to negotiate modification to existing contract)</p> <p>Memo P. G. LaFetre to Kenneth Kasschau dated May 26, 1953</p> <p style="text-align: center;">(If more space is required use separate sheets and attach hereto:)</p>	
<p>11. <u>Contracts, Subcontracts, or Purchase Orders Submitted for Review and Approval:</u> (Furnish brief description of action in this space and attach pertinent documents)</p> <p style="text-align: center;">None</p>	
<p>12. <u>Disputes:</u> Attach a statement summarizing the dispute together with pertinent documents and Background Material.</p> <p style="text-align: center;">None</p>	

UNITED STATES ATOMIC ENERGY COMMISSION
DIVISION OF BIOLOGY AND MEDICINE
WASHINGTON, D. C.

DATE: MAY 2 6 1953

TO : Kenneth Kasschau, Director, Office of Research and Medicine
Oak Ridge Operations Office
FROM : Paul G. LeFevre, Assistant to Chief (Research), Medical Branch
SUBJECT: TRANSMITTAL OF RESEARCH PROPOSAL FOR CONTRACT NEGOTIATION
SYMBOL : BMM:PGL

LeF

This letter with enclosure, in triplicate, is sent in accordance with the procedure described in a letter from the General Manager to all Managers of Operations dated January 27, 1949.

1. Institution: Duke University
2. Investigator (s): See comments
3. Title: See comments
4. () New Contract or (x) Renewal of Contract No. AT(40-1)289
5. Duration - From: July 1, 1953 to June 30, 1954
6. AEC Technical Supervision: Medical Branch
7. Recommended Support: \$19,386.00 (including overhead at 8%)
Authorized by Procurement Directive No. BM53-293
Issued _____ \$ 19,386.00
Activity No. 6300
8. Other Comments:
Project II: Investigator: Dr. Philip Handler
Amount: \$13,705.20
Title: "(a) Localization of Brain Tumors Using Positron-emitting Isotopes
(b) Renal Function and Metabolism"
Project III: Investigator: Dr. J. S. Harris
Amount: \$5,680.80
Title: "A Study of Potassium Metabolism in Isolated Tissue"

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C-3

8. Comments (Continued)

9. Security Requirements:

In accordance with the provisions of GM-93 (Revised March, 1950), and the requirements of the Declassification Guide, the Division of Biology and Medicine has determined that the following security precautions should be taken in connection with the proposed research contract.

Since there is essentially zero chance that restricted data will be required or developed, no personnel security requirements should be imposed.

10. Reports: (x) Reports are to be required as provided for by Memorandum Instruction of November 9, 1949, on subject "Direct Research Contract Reports".

() Special Reports Instructions are as follows:

Enclosures: (x) "A" - Proposal, dated 5/7/53
() "B" - Notification letter, dated
() "C" - Other correspondence, letters
(x) "D" - Procurement Directive BM53-293

Distribution:

Addressee: Original (w encl.) Division File: Yellow Copy (w encl.)
 1st Copy (w encl.) Pink Copy (w/o encl.)
 2nd Copy (w encl.)
Program Analysis Branch File: White Copy (w encl.)
Branch: White Copy (w/o encl.)

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May 7, 1953

Division of Biology and Medicine
Atomic Energy Commission
Washington, D. C.

Gentlemen:

Enclosed are two (2) copies of an application for renewal of contract AT-(40-1)-259 between Duke University and the Commission. Title I, which related to the Fellowship Training Program, was discontinued last year. Title IV, for which Dr. Paul J. Kramer is Project Leader, has been treated individually for the past two years. Title V, for which Drs. I. E. Gray and Karl Wilbur are Project Leaders, will be considered in a separate application to be submitted in the near future by Dr. Wilbur who is presently in the office of the Biology Division of the Commission in Washington. The enclosed application, therefore, is concerned solely with Titles II and III for which Dr. Philip Handler and Dr. Jerome S. Harris are Project Leaders.

Enclosed also are two (2) copies of the annual progress report for Titles II and III of this contract.

I sincerely trust that this application and progress report are in order.

Sincerely yours,



Philip Handler
Professor of Biochemistry
and Nutrition

PH/nlc
Enclosures

1110078

MAY 26 1953

Dr. Philip Handler
Duke University School of Medicine
Department of Biochemistry
Box 3711
Durham, North Carolina

Dear Doctor Handler:

I am pleased to inform you that our Research Contracts Committee has approved continuation of support of your proposal under Titles II and III of Contract AF(40-1)289, for an additional year. The contractual details will be handled through our Oak Ridge Operations Office, and you should hear from a representative of that office within a short time.

The Committee was pleased to note the progress made during the past year, and we trust that the ensuing year will be equally satisfactory.

Sincerely yours,

Paul G. LeFevre
Assistant to Chief (Research)
Medical Branch
Division of Biology and Medicine

~~to~~ to OROO - att: K. Kasschau

LEFEVRE:rmk

Medical

TITLE III

1. Project

a) Project Leader

The work done under this Title will continue to be carried on by the contractor under the direction of Dr. Jerome S. Harris, Professor of Pediatrics and Associate Professor of Biochemistry. Curriculum vitae and bibliography have been previously submitted.

b) Term

The fifth period of performance for this title will commence on July 1, 1953 and will end on June 30, 1954.

c) Nature and Scope of the Problem

The objectives of this title will be: (a) to continue our studies of electrolyte and fluid balance in health and disease and (b) to study the metabolism of renal insufficiency, with particular reference to iron and anemia.

The first objective is a continuation of the general program which has been approached through investigations of potassium metabolism in isolated tissues. As mentioned in the accompanying progress report, time did not permit further clarification of the problem by the use of radioactive potassium, as originally planned. It is now proposed to study, with the aid of radioactive potassium, the equilibrium which exists between surviving tissue slices and their environment. The rates of uptake and discharge of this substance from surviving tissues will be measured and the influence of various conditions on these rates will be determined. From these data, the problem of the existence of Bound or non-exchangeable potassium may be resolved.

The second objective emerged from clinical observations and work done last year on the metabolism of nephrectomized dogs (see Progress Report). It was noted that nephrectomized dogs showed a striking and rapidly developing anemia which did not respond to ordinary therapy. Preliminary observations showed markedly deficient red blood cell formation (as determined by study of radioactive iron uptake) and also increased destruction (by clinical observations on rate of development of anemia). It is proposed to expand these studies by following the plasma disappearance curves of injected radioactive iron into red cells, and the rate of disappearance of cells (labelled with radioactive iron) from the circulation in the hope, ultimately, of gaining some insight into the

TITLE III continued

relationship between uremia and anemia.

2. Budget - Fourth Period: July 1, 1953 - June 30, 1954

a) The Contractor will furnish as its contribution to the project:

1) Salaries of staff members including Project Leader, secretary and several internes and other personnel engaged in this work in excess of the Government's payments under (b) below.

2) Use of laboratories, equipment, facilities and materials on hand as needed.

3) Clerical, administrative and overhead costs in excess of the Government's payments under (b) below.

b) Projected Budget:

1) Personnel

Technician - Mrs. V. Holloway	\$ 3,300.00
Assistant - Mr. E. Forrester	480.00

2) Supplies

(including glassware, isotopes,
chemicals, animals and illustrations,

750.00

3) Equipment

Dubnoff Metabolic Shaker

530.00

4) Travel and Communications

200.00

5) Overhead at 8%

\$ 5,260.00

420.80

\$5,680.80

PROGRESS REPORT

Title III

I. Potassium Exchange in Tissue Slices

The observations recorded in last year's Progress Report have been confirmed and extended. The experiments were performed by the techniques mentioned, using slices of diaphragm, kidney and liver of several species of animals. The slices were introduced into the appropriate medium and incubated either directly or after a preliminary period in chilled saline to leach out much of the potassium. The results are summarized in Table I. The behavior of sodium was usually complementary to that of potassium, while the chloride varied with the sodium. They are, therefore, not included in the table.

Table I

Potassium Concentration of Rat Tissue Slices Incubated in Ringer
Phosphate Containing 5.0 MEQ/L Potassium

Tissue	No. Experiments	Control meq/Kg	After Leaching	Time of Incubation (min.)				
				15	30	60	120	180
Diaphragm	11	87	-	62	-	56	50	51
" (L)*	4	86	25	-	-	40	44	-
Kidney	11	72	-	35	38	37	32	-
" (L)	4	76	16	26	30	34	33	-
Liver	19	93	-	32	31	42	50	-
" (L)	5	97	5	10	11	20	17	-

*(L) Tissue slices "leached" in chilled saline prior to incubation.

Thus, upon incubation in a medium containing 5 meq./l. potassium, diaphragm slices slowly lose potassium to 2/3 of their original content. Thereafter, the concentration remains relatively constant for some two hours. If the potassium content is first decreased by "leaching" to approximately 1/3 of the normal content, muscle will slowly accumulate potassium on incubation to approach the equilibrium value noted after ordinary incubation. This phenomenon is more distinct in kidney slices where there is a rapid initial fall in potassium concentration upon incubation to

approximately 50% of original value. Thereafter, a steady state is achieved for the next hour or more. If the cell potassium is leached to a low concentration by chilled saline, the same value of approximately 50% is quickly reached on incubation in appropriate media.

These results are obviously explicable by a balance between the tendency for potassium to escape from tissues along the concentration gradient from tissues to medium and an active mechanism in the tissues which accumulates potassium in some manner against the gradient. These forces are apparently disturbed by removing and slicing the tissue, as well as by the "unphysiological" medium, etc., so that the normal complement of potassium cannot be maintained. Equilibrium is, therefore, reached at a point where the potassium gradient between cells and medium is less marked. The action of the accumulating mechanism is best seen when the cell concentration of potassium has been lowered by previous leaching.

In the case of liver slices, the balance between the accumulating mechanism and loss of potassium to the medium is more easily disturbed. Ordinarily when the liver is handled rapidly and quickly placed in oxygenated medium at 37° C., the concentration of potassium drops rapidly to approximately 30% of normal. However, the concentration rises on incubation to about 50% of normal - indicating that the accumulating mechanism and/or the escaping tendency of potassium have not been too seriously altered. This is not the case after the liver slices have been leached in chilled saline. Following this treatment, the slices can regain potassium only to a limited extent.

The ability of tissues to maintain potassium concentration is damaged by rough handling, anaerobiosis, cooling, methylene blue and benzimid. It was not appreciably altered by minor changes in the medium, e.g., absence of glucose, or presence of a variety of substrates such as acetate, pyruvate, lactate, glutamate, citrate. Incubation with pitressin, sulfonamides, insulin, or pretreatment of the animal with cortisone, ACTH, sodium bicarbonate (to alkalosis), ammonium chloride

(to acidosis) were without effect. Diamox and caronamide were also without effect, a surprising result in view of the action of benamid. Similar results were obtained with guinea pig and rabbit tissues.

The ability of a tissue to maintain potassium concentration against a tissue-medium gradient is indicated by the ratio at equilibrium of the concentration of potassium in the tissue water to that of the surrounding fluid. Their equilibrium state will be influenced by (a) change in permeability or the "escaping" tendency of potassium from the cells; (b) changes in the potassium accumulating mechanism; and (c) changes in the state of potassium in the cell (bound or unexchangeable potassium). Although we had hoped to approach this problem during the present year by the use of radioactive isotopes, time will probably not permit this to be accomplished. We hope to be able to do this next year. (See request for continuation of grant.)

II. Experiments on the Nephrectomized Dog

Last summer an opportunity to study the metabolism of the nephrectomized dog presented itself. The insight which this might give into problems of fluid and electrolyte metabolism was discussed with Dr. R. F. Poole, at that time a post-doctoral fellow of the Atomic Energy Commission. We hoped that elimination of the selective action of the kidney would permit a better and less distorted view of the translocations of water and salt on alteration of body states. Dr. Poole then began work on this technically difficult problem under my supervision.

The general plan was to nephrectomize dogs bilaterally and to maintain them postoperatively by bi-daily intraperitoneal instillation of a glucose-Ringer solution, followed by withdrawal of the fluid six to twelve hours later (method of Grollman). The electrolyte contents of the fluids given and removed daily were determined so that balances could be calculated. Similar determinations were performed upon the blood at intervals during the post-nephrectomy period.

We have been successful in maintaining dogs for as long as 31 days by this regime of intermittent peritoneal lavage. It quickly became evident that there is a large and steady loss of potassium from the cells in the nephrectomized animal. This amounted to between 2.08 and 2.94 meq. per day, or a total of between 4.7 and 9.5 meq. per kilogram during the entire experiment, depending upon size and duration of the experiment. In most dogs, the losses of potassium took place in a characteristic fashion - rapidly during the first few days, then more slowly and finally increasing rapidly before death. In contrast, sodium was accumulated by these dogs in quite large amounts (9-87 meq. per kilo). There did not seem to be any relation between weight change and sodium gain, but there was a correlation between total amount of sodium gained and the duration of experiment (0.6 per kilo per day for 16 days vs. 3.0 per kgm per day for 24-31 days). In two dogs the balances of Ca, Mg, Cl, PO₄ and NPN were also followed.

Two preliminary experiments were performed to study the effect of alkalosis of the metabolism of these dogs. Alkalosis was produced by doubling the bicarbonate content of the lavage fluids. The elimination of potassium, in which we were particularly interested, was not influenced by the alkalosis which was sufficient occasionally to produce severe tetany.

In addition to the study of water and electrolytes, we were interested in following the blood pressure in these nephrectomized dogs. There is no unanimity on this controversial subject: Grollman believes the hypertension is invariable, while others relate it to the volume of the extracellular fluid. The changes in blood pressure were followed and correlations were attempted between various factors such as weight changes, plasma volume, electrolyte balance.

During the course of this work we were impressed by the striking anemia which appeared and progressed rapidly in all-nephrectomized dogs, despite adequate intake of iron, liver and vitamins. The anemia was only temporarily relieved by whole blood transfusions. This problem was deemed worthy of study, particularly in view of the controversy over the genesis of anemia in humans with poor renal function. To

this end, two dogs have thus far been investigated with the use of radioactive iron. Approximately one week after nephrectomy, a tracer dose of radioactive iron was given intravenously. The disappearance of radioactivity from the plasma and the uptake of the radio iron in the red cells was followed at suitable intervals. From the data obtained, it appears that nephrectomy almost completely prevents the uptake of iron into red cells!! Since the anemia occurs more rapidly than expected even from complete cessation of hematopoiesis, it appears that circulating red cells must be destroyed more rapidly than normal. Combination of these two factors probably explains the rapidly developing anemia, but we are anxious to confirm these results and also to follow the disappearance of transfused radioactive iron labeled cells into nephrectomized. (See request for continuation of grant.)

RECEIVED
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 DIVISION OF BIOLOGY & MEDICINE
 NATIONAL RESEARCH COUNCIL ON HEALTH

Financial Summary

July 1, 1952 - June 30, 1953

Title	Contract	Expenditures to 6/1/53	Expenditures 4th Quarter Estimated	Expenditures Total	Balance Estimated 6/30/53
II	\$ 16,797	\$ 13,093	\$ 3,700	\$ 16,797	0
III	4,622	3,644	1,000	4,622	0
Totals	\$ 21,419	\$ 16,737	\$ 4,700	\$ 21,419	0

PROPOSED BUDGET

SUMMARY

Title	II	III	<u>Total</u>
Personnel	\$ 9,040	\$ 3,780	\$ 12,820
Equipment	1,000	530	1,530
Supplies	2,400	750	3,150
Travel	250	200	450
<hr/>			
Subtotal	\$12,690	\$ 5,260	\$ 17,950
Overhead at 8%	1,015	420	1,435
<hr/>			
Totals	\$19,705	\$ 5,680	\$ 19,385

1110088

APPLICATION FOR RENEWAL

Contract AT-(40-1)-289

between

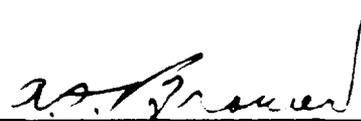
Duke University and the Atomic Energy Commission

May 1, 1953

1110089

ADMINISTRATIVE AUTHORIZATION

This application for renewal of Titles II and III
of Contract AT-(40-1)-289 between Duke University and the
Atomic Energy Commission is hereby approved and authorized.



A. S. Brewer
Business Manager and Comptroller
Duke University

UNITED STATES ATOMIC ENERGY COMMISSION
WASHINGTON, D. C.

Contract Authorization No. EM-55-341

TO : S. R. Sapirie, Manager
Oak Ridge Operations Office

APR 29 1955

FROM : John C. Bugher, M. D., Director, Division
of Biology and Medicine, Washington, D. C.

J. C. B.

SUBJECT : FUND AUTHORIZATION AND TRANSMITTAL OF RESEARCH PROPOSAL FOR
CONTRACT NEGOTIATION

REFERENCE : AEC 102/16 APPROVED OCTOBER 7, 1953, AS IMPLEMENTED BY MEMORANDUM
TO MANAGERS, OPERATIONS OFFICES, DATED OCTOBER 23, 1953, JOINTLY
SIGNED BY THE DIRECTORS OF THE DIVISIONS OF RESEARCH AND
BIOLOGY AND MEDICINE.

SYMBOL : **BMM:FGL**

The research proposal described below has been approved by the
Division of Biology and Medicine, funds are available, and you
are authorized and requested to negotiate a contract in
accordance with the following terms and conditions:

1. Institution: **Duke University**
2. Investigator (s): **Jerome S. Harris, M. D.**
3. Title: **"I. Metabolism and Physiological Role of Potassium;
II. Metabolism of Renal Insufficiency."**
4. () New Contract, (x) Renewal of Contract No. AT(40-1)1646
5. Duration: **7/1/55 through 6/30/56**
6. AEC Technical Representative: **Paul G. LeFevre** *Lef*
7. Funds are authorized for the obligation of this contract
as follows:

<u>Allotment No.</u>	<u>Budget Category</u>	<u>Previous</u>	<u>Amount This Action</u>	<u>Total</u>
<u>06-51-91 (24)</u>	<u>6300</u>	<u> </u>	<u>\$5,300</u>	<u>\$5,300</u>
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8. It is suggested that in the best interests of the government the following type contract be negotiated: **Lump-sum**
9. It is requested that the title to any capital equipment procured under this contract shall be vested with:
- the contractor; the government.

10. Other comments:

The present renewal period is expected to terminate this contract.

Support has been authorized at a level of \$5,300 in new funds plus the unexpended balance of \$1,500, which makes a total operational level of \$6,800.

11. Security Requirements:

In accordance with the provisions of Chapter 3403 of the AEC Manual and the requirements of the Declassification Guide, it has been determined that the following security precautions should be taken in connection with the proposed research contract:

Since there is essentially no chance for the development of restricted data, this project has been placed in Category I as defined in Chapter 3403 of the AEC Manual.

12. Reports: Reports are to be required as provided for by "Revised Guide for the Submission of Research Proposals" dated February 8, 1954.
- Special reports instructions are as follows:

Enclosures: "A" - Proposal, dated _____
 "B" - Notification letter, dated APR 29 1955
 "C" - Other correspondence, none letters

Distribution:

Addressee: Original (w encl.)	Division File: Yellow copy (w encl.)
1st copy (w encl.)	Pink copy (w/o encl.)
2nd copy (w encl.)	
	Branch File: White copy (w encl.)

Program Analysis Branch:
 White copy (w/o encl.)