



NAV1.970527.001

NAVAL DOSIMETRY CENTER
 NAVY ENVIRONMENTAL HEALTH CENTER DETACHMENT
 BETHESDA, MARYLAND 20889-5614

COMMERCIAL: (301) 295-0142

DSN: 295-0142

FAX: (301) 295-5981

To: Don Williams

Company: RECC

Department: _____

FAX Number: (703) 847-0890

Message:

Don - Attached are copies of all the documents we have regarding your recent inquiry to BUMED. My review of these indicates the following:

- NNMC-025: Likely study took place, or at least was started.
- NHPEN-002: Not known if study was performed.
- ONR-31: Not known if study was performed.
- ONR-32: Proposal is for continuation of earlier work which had included human ingestion of N-15 labelled glycine. Not known if this proposal was carried out.
- NMRU2-14: Study appears to have been carried out since a published journal article resulted. Article not available so study details unknown.

Hope this helps. Call if questions.

From: CAPT KARL MENDENHALL

Date: 5/7/97

Number of Pages: 19
 (Including cover sheet)



Department of Defense
Radiation Experiments Command Center
 6801 Telegraph Road
 Alexandria, Virginia 22310-3398

Capt Rick LaFontaine
 Undersea Medicine and Radiation Health
 Bureau of Medicine and Surgery
 2300 E Street, NW
 Washington, DC 20372

Over the last several months, the RECC has been in the process of preparing Volume 2 of the book for final layout. During this process, we discovered a few problems that need your attention. It is unclear from the documentation for events NNMC-025, NHPEN-002, ONR-31, and ONR-32 that the study actually took place. Please review the materials and determine if the study was performed. In addition, it is unclear if event NMRU2-14 involved any radiation exposures. Please review the documentation and determine what the radiation exposure was, if any.

We request that you provide a response by Friday, 9 May 1997. If you have any questions, contact Don Williams (703) 749-8754 or Chris Mahoney (703) 917-5439. Thank you for your assistance with this matter.

FOR THE DIRECTOR:

*Thanks again Rick
 C. B. J.*

[Signature]
CLAUDE BAILEY, JR.
 Colonel, AG, USA
 Deputy Director,
 Command Center

OPTIONAL FORM 99 (7-80)

FAX TRANSMITTAL		# of pages ▶
To CAPT MENDENHALL	From CAPT LA FONTAINE	
Dept./Agency NAVAOSGEN	Phone # (202) 762-3447	
Fax # (301) 295-5981	Fax # (202) 762-0731	

Study # NHPEN-02: **Clinical Study of Intraocular Lenses**

Location: NH Pensacola

Date: Unknown

Primary

Researchers: E. A. Novak

Sponsors: N/A

Human

Subjects: 0 patients - special class of patients is N/A

Purpose: To assess the risk of using intraocular lens to replace the crystalline lens following cataract surgery, by maintaining preoperative, operative and postoperative records to allow evaluation of adverse effects

Category: Other

Records: NH Pensacola

Classification: Unclassified

CIP - NNMC - ENCL (116)

Done 5-4-94

NNML-24

* RADIOISOTOPIC DETERMINATION OF GLOMERULAR FILTRATION RATE (GFR) AND EFFECTIVE RENAL PLASMA FLOW (ERPF). G.J. Weir, Jr. Naval Hospital, Great Lakes.

Determination of ERPF has not become a common clinical aid because of the difficulty of chemical determinations of para-aminohippuran. Clinical GFR determinations are approximated by creatinine clearance because of similar problems with inulin. This necessitates 24-hour urine collections, an error-prone procedure.

A technique has been developed which permits determination of ERPF and GFR, alone or simultaneously, from the plasma disappearance curves of radioactive compounds. No urine collections are necessary. A single injection of the radioactive compound is utilized. Determinations require approximately two hours of patient time and six blood samples at specified times following injection.

Using this technique 25 measurements were made on 17 normal people. ERPF was 561 ± 115 ml/min (mean \pm standard deviations), GFR 190 ± 47 ml/min (both values corrected to 173 m^2 body surface area).

CICC 2-13-009

Done 5-4-94

NNMC-25

THE ROLE OF THYROTROPIC HORMONE (TSH) IN SIMPLE AND MULTINODULAR GOITER AND IN THYROID CARCINOMA. G.J. Weir, Jr. and R.W. Spath. Naval Hospital, Great Lakes.

A radioimmunoassay for TSH is being developed and will be used to evaluate the role of TSH in the pathogenesis of goiter and to evaluate the efficacy of thyroid replacement therapy.

Arrangements have been completed for the principal investigator and a technician to learn the technique of TSH radioimmunoassay at a laboratory currently performing the study. Serum samples from patients with goiter and thyrotoxicosis have been saved for future analysis.

CICC 2-13-013

* DIAGNOSIS OF EARLY ARTHRITIS BY JOINT SCINTIPHOTOGRAPHY. G.J. Weir, Jr. and R.H. Easterday. Naval Hospital, Great Lakes.

Joint scintiphotography $^{99\text{m}}\text{Tc}$ pertechnetate demonstrates nonspecific abnormalities in joints involved with arthritic conditions. The pattern of joint scintiphotography in early arthritis is being evaluated.

Studies of normal joints in patients undergoing brain scanning reveals a pattern of relative lack of activity in

the proximal palm and in the knee joint region immediately following injection of pertechnetate. At 30 minutes postinjection the pattern of activity is more homogeneous.

CICC 2-13-014

Done 5-4-94

NNML-27

* DIAGNOSIS OF URINARY TRACT OBSTRUCTION BY SCINTIPHOTOGRAPHY. G.J. Weir, Jr.; K.R. Hutchins and J.E. Keeton. Naval Hospital, Great Lakes.

The possibility of diagnosing and localizing urinary tract obstruction by scintiphotography, especially using newer agents with high photon flux is being evaluated.

Scintiphotographs of the kidneys are obtained for up to two hours following the injection of ^{131}I -Hippuran and/or $^{99\text{m}}\text{Tc}$ -iron ascorbate acid complex. The scintiphotographs are evaluated without knowledge of the clinical status of the patient. In addition to routine scintiphotography, a Super-8 movie camera is being evaluated as a recording medium. Two patients have been studied to date. In one a ureteropelvic junction obstruction was correctly diagnosed from routine Polaroid scintiphotos. Renography and renal scintiphotography were normal on the second patient. Intravenous pyelography was also normal and the final diagnosis excluded urinary tract obstruction.

CICC 2-13-017

Done 5-4-94

NNMC-28

DYNAMIC SCINTIPHOTOGRAPHY IN THE EVALUATION OF RENAL DISEASE. G.J. Weir, Jr. Naval Hospital, Great Lakes.

Dynamic scintiphotography using a variety of radio-nuclides including $^{99\text{m}}\text{Tc}$ pertechnetate, ^{131}I -Hippuran and $^{99\text{m}}\text{Tc}$ -iron ascorbate complex may be of value in differentiating renal cysts and tumors and in evaluating renal parenchymal disease. Studies are being performed using a persistence scope attachment to the gamma camera and 8-mm film. The equipment has just been installed.

In one patient studied using routine scintiphotography an inflammatory mass was present as an area of decreased activity using both ^{131}I -Hippuran and the $^{99\text{m}}\text{Tc}$ -iron ascorbate complex.

CICC 2-13-018

#

Study #NNMC-25: The Role of Thyrotrophic Hormone (TSH) in Simple and Multi Nodular Goiter and Thyroid Carcinoma.

Location: Naval Hospital Great Lakes

Date: 1972

Primary

Researchers: G. J. Weir , R.W. Spath

Sponsors: Dr. J. F. Wilber, Northwestern University

Human

Subjects: None, in vitro study

Purpose: To develop a radioimmunoassay for TSH to evaluate the role of TSH in the pathogenesis of goiter and to evaluate the efficacy of thyroid replacement therapy.

Category: Other, Clinical Research

Records: U. S. Navy Medicine, Vol. 59 No. 6, June 1972

Classification: Unclassified

85-08-2083-00

PROTOCOL

NH PEN #02

INVESTIGATIONAL PLAN

I. BACKGROUND AND OBJECTIVES OF PROPOSED RESEARCH PROGRAM

The use of intraocular lenses to replace the crystalline lens following cataract surgery was introduced in England by Ridley in 1949. Initially, intraocular lenses were received with great enthusiasm; however, because of their large size and heavy weight, numerous complications with these original lenses soon began appearing. It is estimated that 25% of the original Ridley lenses had to be removed. This high failure rate very quickly led to the abandonment of intraocular lenses.

Throughout the world the idea of replacing the crystalline lens with some form of intraocular lens, notwithstanding the failure rate of Ridley, remained a very attractive concept. More and more researchers looked at the 75% success rate of Ridley rather than his 25% failure rate. In doing so, they began to develop smaller, thinner and lighter intraocular lenses.

It is estimated that these newer lens designs coupled with improved surgical techniques have been successfully used in over 100,000 cases. As a result, these patients have enjoyed the benefits of more normal vision without the encumbrances normally associated with cataract surgery. In effect, these patients enjoy a visual quality of life approaching that enjoyed prior to their development of cataracts. As a result of the above, intraocular lenses have enjoyed an ever-increasing popularity with both the patients and ophthalmological community. These newer lens designs have not, however, been free of problems. There have been isolated reports of complications and in some instances, severe adverse reactions necessitating removal of the intraocular lens from the eye. However, without precise corresponding information on the occurrence of these adverse reactions, it is impossible to assess reasonably the risk associated with intraocular lens implantation as compared with non-implanted surgery.

In this context, the objectives of the proposed research program are as follows:

- 1) To determine postoperative visual acuity of patients receiving an intraocular lens, and compare these results with those of a control group of patients who undergo cataract surgery but do not receive an intraocular lens;
- 2) To describe the occurrence and time course of post-operative ocular complications and adverse reactions both for intraocular lens implant subjects and for control subjects;
- 3) To compare the occurrence of adverse reactions and ocular complications in the implant group and in the control group, in order to delineate any significant differences;
- 4) To describe the occurrence of postoperative lens complications for the implant group, and their relationship to ocular complications;

LAN

- 5) To identify subgroups within the implant study population that are at "high risk" of particular complications, as compared to the control group.

INVESTIGATION

In order to accomplish these research objectives, a clinical trial design, based on the guidelines recommended by the FDA Ophthalmic Advisory Panel, has been developed. The clinical trial design incorporates the Core Investigator/Adjunct Safety Study concept previously reviewed by FDA staff and selected members of the Advisory Panel.

The remaining sections of this appendix provide details of the study design, as well as the plan for the final analysis and presentation of the results.

II. PATIENT POPULATION

The population for this study (both implant and control subjects) will be patients who would ordinarily be considered eligible for intraocular lens implantation according to the following criteria for inclusion (indications) and criteria for exclusion (contraindications):

CRITERIA FOR INCLUSION: INDICATIONS

1. Monocular Cataract.
2. Monocular Cataract unable to wear contact lenses.
3. Physically handicapped patients (unable to handle contact lenses).
4. Cataract with concomitant macular degeneration.
5. Special vocational or avocational needs requiring uncorrected (spectacles or contact lenses) usable single binocular vision.

CRITERIA FOR EXCLUSION: CONTRAINDICATIONS

1. Poorly controlled glaucoma.
2. Proliferative diabetic retinopathy.
3. Rubella cataract.
4. Chronic severe uveitis.
5. Corneal endothelial dystrophy.
6. Very shallow anterior chamber.
7. Insufficient iris to allow fixation of lens (Aniridia).
8. Any eye disease producing an inflammatory reaction in the eye.
9. Chronic iritis.
10. Previous history of or predisposition to retinal detachment.

Study # -ONR-31: Distribution and Turnover of Sodium and Potassium in Acute Infections

Location: Wake Forest College

Date: May 1948

Primary

Researchers: Dr. George T. Harrell

Sponsors: Office of Naval Research, Contract No. NR 171 677

Human

Subjects: Unknown

Purpose: To study the distribution and turnover of sodium and potassium in acute infections.

Category: Clinical Research

Records: Procurement Justification, Office of Naval Research, NR 171 677
Contract to Wake Forest College. Re: Distribution and Turnover
of Sodium and Potassium in Acute Infections.

Classification: Unclassified

NAVEXOS-2770

PROCUREMENT JUSTIFICATION
Office of Naval Research
Research Group

Security Class Uncl.

NR 171 877

Date 19 May 1948

Project Designation No.

Contract No.

Task Order

M. G. Sheleanyak
ONR Scientific Officer

LEAVE BLANK.	
Procurement Directive Number	
Research Navy Appropriation 1780317	
Object Classification	Exp. Acct. No.

Wake Forest College
Contractor.

Dr. George T. Harrell
Principal Investigator

Est. Man-Years: Prof: 1 Grad. Stud: 2

Distribution and turnover of Sodium and Potassium in Acute Infections.

Est. Expenditures (thousands):		Est. Compl. Date Total Project
Past	Future	
'46	'49	
'47	'50	<u>contg.</u>

Project title

Can any gov't agency do this work in the time desired? no

THIS COMMITMENT: subsistence and travel
 Basic: \$ 9,500 / AEC (Est.)
 Applied: (Est.)
 Est. Cost: \$ 9,500 AEC (1948 Funds)

REPORTS required: FINAL and

6 STATUS: Quarterly or

30 Scientific and/or Technical

X Others: As requested or at discretion of

contractor, manuscripts submitted for

Duration: From 7/1/48 publication

To 30 June 1949

Why was this contractor selected?

Dr. Harrell the principal investigator of this project is well qualified through considerable past experience in the general field to carry out these investigations.

Interested agencies, correspondence not attached, etc.

Division of Biology and Medicine, Atomic Energy Commission.

APPROVED:

(3) T. J. Killish, Science Director, Research

(1) Head, (Acting) Biophysics Branch

(4) W. H. Leahy, Asst. Chief for Research

(2) Director, Medical Sciences Division

(5) C. M. Bolster, Deputy and Asst. Chief of Naval Research

Enclosures (A) Original copy of proposal & contractor's business office approval
(B) Justification and Brief (Use reverse side)

(Submit Original & 4)

JUSTIFICATION AND BRIEF

NR 171 677

Include: (1) Brief of Project (2) Scientific Justification (3) Possible Naval Application

Director: DR. ROBERT H. ...

(2)

Serum sickness will be induced in animals. When edema develops, radiosodium and thiocyanate could be given. The plasma, urine, and interstitial fluid for total sodium would be compared with radio sodium and correlated with thiocyanate space. A similar experiment will be done administering radioactive potassium. The experiments will be repeated with human beings.

Studies in human beings with certain diseases have shown a drop in the blood volume and a rise in the thiocyanate extravascular space. It is not known whether edema is within or between cells. Knowledge of the reactions and their causes would be obtained through these studies.

The investigations may provide information which could be utilized in the treatment of certain diseases in Naval medicine.

It is requested that the contracting officer indicate to the contractor the desirability of assigning certain Naval personnel, either Regular or Reserve, or such other personnel as the Navy or other agencies associated with the Navy on a project, (e.g. AEC), may deem desirable to duty in connection with the investigations to be conducted by the contractor for the purpose of receiving instruction in this type of work. It is understood that such assignments will be made only with the full consent of the contractor.

Study # -ONR-32: Investigation of Protein Synthesis by Use of the Isotope N-15

Location: Tulane University

Date: 1948

Primary

Researchers: Unknown, Cooperation with Dr. William Parson

Sponsors: Office of Naval Research (Unknown if work was funded. Abstract based on research proposal.)

Human

Subjects: Unknown

Purpose: To continue and enlarge an investigation in protein metabolism.

Category: Clinical research.

Records: Research Proposal for the Investigation of Protein Synthesis by Use of the Isotope N-15, 1948

Classification: Unclassified

PROCEDURE FOR THE INVESTIGATION OF PROTEIN SYNTHESIS BY USE OF THE ISOTOPE N-15

TULANE UNIVERSITY

The current proposal is to continue and enlarge primarily the physical aspects of an investigation in protein metabolism by the use of stable isotopes in the Biophysics Laboratory of Tulane University.

PRESENT STATUS OF THE PROBLEM

In a cooperative venture with the Department of Medicine, Surgery and Physiology, of the Tulane University Medical School, a preliminary investigation into protein metabolism in man has been made. The physical procedure, as well as the fundamental interpretation of such results as were forthcoming, have been the responsibility of the Biophysics Laboratory. Human subjects, kept in nitrogen equilibrium, that is, with an equal input and outgo of nitrogen, were fed a single test meal containing an amino acid, glycine, labelled with an excess of N-15. The subsequent excretion of N-15 was then followed over a three- to five-day period. The measured dilution of the N-15 excreted was then compared with the N-15 dilution predicted on the following simple assumptions.

Let: N_1 - amount of Nitrogen ingested

N_e - amount of Nitrogen excreted

N_x - amount of Nitrogen in the body exchangeable with ingested Nitrogen

N_{15} - amount of ingested N-15

N_{e15} - amount of N-15 excreted

p - a factor which is a function of time and the measure of the proportion of previously ingested nitrogen which has entered the cycle characterized by the N_x to the total amount of nitrogen ingested over the period of observation.

Then one may write Equation 1:

$$N_e^{15} = pN_1^{15} \frac{N_e}{pN_1 + N_x} + N_1^{15} \frac{N_e}{pN_1 + N_x}$$

and the term from the right hand side of the equation

$$\frac{pN_e}{pN_1 + N_x} \quad \text{equals a dilution factor,}$$

$$\text{or } D_f = \frac{N_e^{15}}{N_1^{15}} = \frac{pN_e}{pN_1 + N_x} \quad \text{Equation 2.}$$

The dilution factor may be obtained from an analysis of the samples of excreted nitrogen and the ingested nitrogen with the mass spectrometer.

One may then solve Equation 2. for $\frac{N_x}{p}$.

$$\frac{N_x}{p} = \frac{N_e}{D_f} - N_1 \quad \text{Equation 3.}$$

Thus, it has been possible to measure the quotient $\frac{N_x}{p}$.

N_x may then be defined as the amount of body nitrogen into which a fraction "p" of the test glycine has been assimilated. The factor p is a function of time and represents the portion of the test meal that, within the time of observation, has entered into the metabolic process studied.

Assuming p to be constant, the N_x has been studied as a function of time and over the three days which it has so far been possible to study it increases logarithmically with time, that is:

$$N_x(t) = N_{x0} e^{+nt}$$

where n may now be defined as the assimilation coefficient for the metabolic processes investigated.

In patients with adrenal disturbances subject to endocrine therapy, significant variation in N_x and n have already been discovered.

PROPOSAL FOR CONTINUATION OF WORK

1. A modified experiment is to be performed for the elimination of the factor p . In the previous work, the metabolic nitrogen into which the test meal was assimilated was termed N_x . Actually measured was the factor $\frac{N_x}{p}$ where p designated the fraction of test meal nitrogen 15 that had entered the N_x "pool" in the time of observation. The factor p is therefore dependent on time in such a way that if there is no time difference in the isotopic ratio of the nitrogen taken in the diet, p becomes unity and may be eliminated.

To do this, requires that the subject be kept on a diet in which the N-14 --N-15 ratio is constant with a fairly high excess of N-15, about 10 atom-percent. Each experiment would require from three to five days for the subject to reach equilibrium. By such an experiment variation in p may be distinguished from variation in N_x with time and the true value of n , an assimilation coefficient, be more nearly determined.

2. The change of N_x with time over short periods of observation (three to five days) was found to be represented by:

$$N_x(t) = N_{x0} e^{-\lambda t}$$

But obviously, the maximum value of N_x is something less than the total weight of Nitrogen in the subject. There must be a second term in the

~~Left side of the above equation which would describe the dissimilation or breakdown of nitrogen, could only be followed isotopically when~~

enough tracer was introduced to go through the whole metabolic cycle without too great dilution. For this purpose, the continuous feeding experiment described above should be adequate.

3. It is desirable to measure N_x and n not only for glycine, but other amino acids as well. These may be obtained in the biologically active isomeric form by using yeast as a biological synthesizing medium in which the only source of nitrogen available to the yeast would be an ammonium salt enriched with N-15. Here the improved sensitivity which we expect from the new design of a mass spectrometer (described under facilities for investigation) is important.

4. The limit of the sensitivity of a technique involving the new spectrometer will be the natural variation and the relative abundance of the stable isotopes of nitrogen. Various figures for this variation are currently recorded. It has been our experience that at least a portion of this variation is due to the formation of methylamine in the digestion process. We should like, therefore, to undertake a more extensive investigation into the procedures for the digestion of protein in the preparation of nitrogen with the object of circumventing such procedures as may cause apparent variations in the N-15 concentration.

~~Since there is no hazard in the isotope procedure itself, we plan to use laboratory personnel as normal experimental subjects. We wish to continue~~

~~these investigations in man, for quite apart from any fundamental information that we may gain from such studies, there are purely empirical~~

* COMPLETION
OF TRANSMISSION *
(4 PGS INCLUDING COVER)



NAVAL DOSIMETRY CENTER
NAVY ENVIRONMENTAL HEALTH CENTER DETACHMENT
BETHESDA, MARYLAND 20889-5614

COMMERCIAL: (301) 295-0142
DSN: 295-0142
FAX: (301) 295-5981

To: Don Williams
Company: RECC
Department: _____
FAX Number: (703) 847-0890

Message:

Don - Attached are copies of all the documents we have regarding your recent inquiry to BUMED. My review of these indicates the following:

- NNMC-025: Likely study took place, or at least was started.
- NHPEN-002: Not known if study was performed.
- ONR-31: Not known if study was performed.
- ONR-32: Proposal is for continuation of earlier work which had included human ingestion of N-15 labelled glycine. Not known if this proposal was carried out.
- NMRU2-14: Study appears to have been carried out since a published journal article resulted. Article not available so study details unknown.

Hope this helps. Call if questions.

From: CAPT KARL MENDENHALL

Date: 5/7/97

Number of Pages: 19
(Including cover sheet)

increased intensity of the ion beam. It has also been designed to have about twice the inherent stability of the present spectrometer.

The Biophysics Laboratory also has the usual facilities for the digestion of proteins and the liberation of nitrogen required for analyses with the mass spectrometer. In addition the Laboratory has an ultra-centrifuge and electrophoresis equipment useful for the separation of small amounts of proteins from complex mixtures. The Laboratory has quite complete facilities for investigations with radioactive material.

The Laboratory has its own shop facilities and mechanician, complete provisions for electric and electronic instrumentation and so forth.

PERSONNEL

Upon completion of the spectrometer (June 30, 1949) the personnel now engaged in the design and construction of it will be available for the work here proposed. This includes the Director of the Biophysics Laboratory, Dr. Robert Nieset, about 1/3 time; Walter G. Byrne, Research Associate in Biophysics, 1/2 time; the full time of one biophysics technician whose principal training has been in physics. Assistance and consultation in purely biochemical aspects is available through the Department of Biochemistry of Tulane University Medical School.

In the endocrinological aspects of the metabolic problems to be attacked the advice and direction of Dr. William Parson, now of the Ochsner Clinic and Tulane Medical School with whom work is currently in progress, will be continued even though he goes to the Medical Department of the University of Virginia in June 1949. Plans for close coordination in the investigations of endocrine factors in nitrogen metabolism between his group and the Biophysics group at Tulane have been worked out.

REQUIREMENTS FOR THE INVESTIGATION

Personnel:	1 Research Associate (Physics) 1/2 time\$2250 a yr.
	1 Technician (Physics) full time\$2500 a yr.
	1 Physical Director, 1/3 time\$2500 a yr.
Materials:	One year's supply of N-15\$3000
	Chemicals and chemistry lab. supplies\$1000
	Mechanical and electronic instrumentation	
	and supplies\$1000
	Travel, communication, publication\$ 500
	Overhead, 20% of salary\$1450
		<hr/>
	Total	\$14,200

Study# NMRU2-14: Preliminary Observations on a New Disease in Man - Intestinal Capillariasis

Location: NMRU2 (Manila)

Date: 1972

Primary

Researchers: Dizon, J. J., Watten, R. H.

Sponsors: Department of Public Health, Philippines and NMRU 2.

Human

Subjects: Unknown

Purpose: Investigated physiological changes due to intestinal capillariasis. Study showed patients had severe malabsorption of fats and sugars and a protein-losing enteropathy.

Category: Other, clinical research.

Records: J. Philippine Med Assn 1969; 45: 5-20.

Classification: Unclassified