NAV1.960102.002

BUMED-712:r
3900
20 DECEMBER 1971

VIA : CODE 712
CODE 7, 71
CODE 10

USE OF HUMAN VOLUNTEERS IN CONNECTION WITH C-1-C-C STUDY 2-48-202 ENTITLED "APNEIC OXYGENATION IN ANESTHESIA"; REQUEST FOR APPROVAL OF

EN (1) CO, NH, OAKLAND LTR 78:BB; 3900:6401 DTD 2 DEC 71

1. SUBJECT REQUEST FOR APPROVAL OF HUMAN VOLUNTEERS IN C-1-C-C STUDY 2-48-202 IS READDRESSED FOR APPROPRIATE ACTION.

VERY RESPECTFULLY,

R. L. BERNSTINE

NAVSO 5216/5 (7 3) S/N 0104-904-1750

UNITED STATES GOVERNMENT

Memorandum

DEPARTMENT OF THE NAVY

BUMED-712:FBN
3900
DATE : 13 DECEMBER 1971

FROM : CODE 712

TO : CODE 10

SUBJECT : USE OF HUMAN VOLUNTEERS IN CONNECTION WITH A STUDY ON APENIC OXYGENATION IN ANESTHESIA

ENCL : (1) CO LTR 78:BB, 3900:6401 OF 2 DEC 71

1. PLEASE REVIEW ENCLOSURE (1) TO DETERMINE WHETHER THE HAZARDS IN "APENIC OXYGENATION IN ANESTHESIA" ARE SUCH AS TO REQUIRE APPROVAL FOR HUMAN VOLUNTEERS FROM SECNAV IN ACCORDANCE WITH SECNAVINST 3900.39 DTD 28 APR 69.

VERY RESPECTFULLY,

RLBernstine
R. L. BERNSTINE

for 12-15-71

NAVAL HOSPITAL

78:bb
3900:6401
2 Dec 1971

From: Commanding Officer, Naval Hospital, Oakland, California
To : Secretary of the Navy
Via : Chief, Bureau of Medicine and Surgery (Code 7)
Chief of Naval Personnel
Commandant of the Marine Corps

Subj: Use of human volunteers in connection with study on Apenic Oxygenation in Anesthesia; request for approval of

Ref : (a) Art. 1-11 MMD
(b) SecNavInst. 3900.39 dtd 28 April 1969
(c) CICC research protocol number CICC 2-48-202 dtd 1 Sep 1971

Encl: (1) Copy of RDT&E volunteer form.

1. Approval for use of volunteers, military personnel, active and retired, and dependents of military personnel as requested in connection with subject study.

2. All test subjects will be true volunteers and all necessary precautions will be taken to protect the individuals concerned.

3. Forms of consent will be obtained from patients prior to their inclusion in this study.

H. P. MAHIN

SAMPLE FORM

28 April 1969

RDT&E ACTIVITY

CONSENT TO PARTICIPATE VOLUNTARILY IN A RESEARCH, DEVELOPMENT, TEST, OR EVALUATION (RDT&E) PROCEDURE

DATE _____

1. I hereby volunteer to participate as a subject in an RDT&E procedure being conducted under Element No. _____, Project No. _____, Work Unit Title "_____", which has been approved by _____ (sponsoring command). I understand that the adequacy of safety measures has been certified by the Chief, Bureau of Medicine and Surgery, and that authority to use human volunteers has been granted by the Secretary of the Navy.

2. The nature and purpose of the procedures have been explained to me as follows: (See attached summary.)

3. In making my decision to volunteer, I am not relying upon any information or representation not set forth in this document, or attached summary. My consent is given as an exercise of free will, without any force or duress of any kind. I understand that my consent to participate does not constitute a release from any possible future liability by the United States attributable to the experiments.

SIGNED: _____

_____
(TYPED NAME, RANK, RATE, OR GRADE)

DATE OF BIRTH _____

WITNESSED: _____
(NOT DIRECTLY INVOLVED IN TEST)

APPROVED: _____

_____
(TEST DIRECTOR)

Copy to:
Service record, jacket, or personnel file

Enclosure (1)

INSTITUTION: U. S. Navy Investigation Center
Naval Hospital
Oakland, California 94627

TITLE OF PROJECT: Apneic Oxygenation in Anesthesia

INVESTIGATORS:

PRINCIPAL: H. Dean, CAPT MC USN
Chief, Anesthesiology Service
Percent of time available for study: 2%
Projected rotation date: July, 1972

ASSOCIATE:

J. L. Steffer, LCDR MC USN
Staff, Anesthesiology Service
Percent of time available for study: 8%
Projected rotation date: July, 1973

R. L. Fraioli, LT MC USN
Resident, Anesthesiology Service
Percent of time available for study: 10%
Projected rotation date: August, 1972

L. A. Sheffer, LCDR MC USN
Staff, Anesthesiology Service
Percent of time available for study: 10%
Projected rotation date: July, 1975

PLANNING ESTIMATE:

	Current FY '72	CFY + 1	CFY + 2
Direct Man Years	.30		
MILITARY	.30		
CIVILIAN			

FUNDS - TOTAL	2,580
BUMED-CIP	1,330
OTHER	None
INVESTMENT EQUIPMENT	1,250

CLINICAL INVESTIGATION PROGRAM

MED-6000-4

ACTIVITY Naval Hospital, Oakland DATE 1 September 1971

BUMED CICC STUDY #IP '72-4

ANNUAL RESOURCES TARGET TOTAL SUMMARY

STUDY TITLE: Apneic Oxygenation in Anesthesia

PRINCIPAL INVESTIGATOR:
H. Dean, CAPT MC USN
Chief, Anesthesiology Service
Percent of time available for study:
Projected rotation date: July, 1972

ASSOCIATE INVESTIGATORS:

J. L. Steffenson, CDR MC USN
Staff, Anesthesiology Service
Percent of time available for study: 8%
Projected rotation date: July, 1973

R. L. Farioli, LT MC USN
Resident, Anesthesiology Service
Percent of time available for study: 10%
Projected rotation date: August, 1972

L. A. Sheffer, LCDR MC USN
Staff, Anesthesiology Service
Percent of time available for study: 10%
Projected rotation date: July, 1975

DIRECT PERSONNEL RESOURCES REQUIREMENTS IN MAN YEARS

		PRIOR FY	CURRENT FY '72	BUDGET FY	BUDGET FY +1
MILITARY	CAPT MC (0020) CDR MC (0613) LCDR MC (0613) LT MC (0613)		.30		
CIVILIAN PROFESSIONAL					
CIVILIAN SUPPORTING					
	TOTALS		.30		

DIRECT O&M Funds Required	$1,305
Direct Minor Construction/ Facilities Funds Required	None
DIRECT Investment (OPN) Equip Funds Required	$1,250

BUMED CICC NUMBER: CIP '72-4
(BUDGET FY + 1) 1 September 1971

MED-6000-4

CLINICAL INVESTIGATION STUDY RESOURCE REQUIREMENTS FOR FY '72

DESCRIPTION	from	1 Sept. '71 through 30 June '72		
DIRECT PERSONNEL	Time or Effort % / Hours	Amount Re[illegible]		
NAME TITLE OF POSITION		SALARY	FRINGE BENEFITS	TOTAL
a.				

CONSULTANT COSTS: None

INVESTMENT
EQUIPMENT ITEMS:
Calculator c Sg. Route Capability, Freiden (To be used for statistical computation--using formulas) $1,250.00

SUPPLIES: *
Introcasts-needles, stopcock $200.00
Gases 100.00 $ 300.00

NONINVESTMENT EQUIPMENT ITEMS:
None

PUBLICATION COSTS: Graphs and Illustrations (6) $300.00
Reprints: 200 at $65.00/100 = 130.00
Miscellaneous clerical supplies 25.00 $ 455.00

ALTERATIONS & RENOVATIONS:

None

TRAVEL:
Presentation at ASA $ 500.00

OTHER EXPENSES:
Maintenance contract on calculator $ 75.00

a. Personnell for editorial and clerical assistance included in CIP '72-1

O&M 1,330
[illegible] 1,250

A. PROJECT TITLE: Apneic Oxygenation in Anesthesia

B. PRINCIPAL INVESTIGATOR: Captain H. N. Dean (MC) USN

C. ASSOCIATE INVESTIGATORS: Commander J. F. Steffenson (MC) USN
Lieutenant Commander L. A. Sheffer (MC) USN
Lieutenant R. L. Fraioli (MC) USN

D. OBJECTIVES: The objective will be to measure (1) changes in PaO_2 in an open system with oxygen being supplied by a nasopharyngeal catheter, (2) rate of oxygen inflow, (3) changes in R/Q, (4) changes in pulmonary shunt fraction, and (5) changes in lung volume (FRC) as related to the length of apneic oxygenation.

E. BACKGROUND: The technique of apneic oxygenation (supplying oxygen to the upper airways of patients who are not breathing) has long been used in anesthesia for various types of surgical procedures, such as direct laryngoscopy, tonsillectomy and bronchoscopy. Many studies investigating the respiratory and cardiovascular effects of this technique have been done and valuable information obtained. However, there are some aspects of apneic oxygenation that have not been evaluated and are of critical importance to the technique.

F. APPROACH: Patients selected for the study will be divided into three groups of eight patients each. All patients will be normal, healthy volunteers who will be required to have normal pre-operative chest X-rays, ECG, CBC, urinalysis, and pulmonary function studies. All patients will be informed as to the nature of the study and to the risk involved. They will be asked to sign a consent allowing us to place a radial artery catheter for blood sampling. All patients will be connected to an ECG monitor. Frequent recording of blood pressure and heart rate will be taken by an anesthesiologist. No premedication will be given.

GROUP I: Patients in Group I will be scheduled for elective surgery confined to an extremity. They will receive a regional anesthetic for surgical anesthesia. With the patient awake and cooperative, a functional residual capacity (FRC) will be determined using the helium dilution technique. The patient's R/Q will be determined as follows: The patient will breathe 100% O_2 from the reservoir of a Godart respirometer. He will then exhale into a bag-in-a-box system whose volume will be measured by the displacement principle. The exhaled gas will then be analyzed for pCO_2 by a CO_2 electrode and the total amount of O_2 and CO_2 in the exhaled volume calculated. This will provide for the amount of CO_2 exhaled and the amount of O_2 exhaled and the amount of O_2 used by the patient resulting in the R/Q. The patient will then be given a bolus of sodium pentothal (5 mg/kg) to induce anesthesia. With the patient breathing spontaneously under pentothal anesthesia, another FRC will be determined. The patient will then be given a bolus of succinylcholine (1 mg/kg) and intubated with an orotracheal tube. He will then be kept anesthetized and paralyzed with a 0.2% pentothal drip and a 0.2% succinylcholine drip, respectively. After manual ventilation with 100% oxygen for five minutes an arterial blood gas sample will be taken, and the apneic period of apneic oxygenation will begin. During the period of apnea, a supply of 100% oxygen will be provided from the Godart Reservoir so that oxygen inflow may be measured during the apneic period. Arterial blood samples will be taken at one minute intervals until the apneic period is completed. These samples

will be analyzed for [illegible] pO_2, and pCO_2 on an IL 113-27. Once the patient has [illegible] spontaneous [illegible] study concluded.

From the arterial pO_2 values obtained the arterial-alveolar oxygen gradients will be determined as a reflection of the V/Q as follows:

Alveolar pO_2 equals 760 mmHg (mmHg water vapor pressure plus pCO_2)
Arterial pO_2 equals PaO_2 measured.

Changes in lung volumes (FRC) during the apneic period will also be calculated from measurements of R/Q, pCO_2, and oxygen utilization.

GROUP II: Patients in Group II will be those patients having elective direct laryngoscopy where general anesthesia is required. These patients will be anesthetized with a bolus of pentothal followed by 0.2% pentothal drip. They will be breathing 100% O_2 via mask. Paralysis will be achieved by a 0.2% succinylcholine drip. Once paralysis is [illegible]d and the laryngoscopist is ready to begin, the mask will be removed and 12 [illegible]r. nasal catheter will be placed into the nasopharynx and 100% oxygen delivered through it. Again, arterial blood samples will be taken at apnea and every minute thereafter. These will be analyzed for pH, pO_2, and pCO_2. Arterial-alveolar oxygen gradients will also be determined.

GROUP III: Patients in Group III will serve as the control group. These patients will be scheduled for elective surgery confined to an extremity. They will then breathe 100% oxygen via mask for five minutes and anesthetized with a bolus of pentothal followed by a 0.2% pentothal drip. They will be paralyzed with a 0.2% succinylcholine drip to be rendered apneic. The mask will then be removed and only air allowed to fill the upper airways. Again, arterial blood samples will be taken at apnea and every one minute thereafter until the period of apnea is completed. Arterial-alveolar oxygen gradients will also be determined for this group.

The period of apneic oxygenation will be discontinued at such time that any of the following occur: untoward changes in cardiovascular status, pCO_2 rises to 70 mmHG, pO_2 falls to 100 mmHg.

At the conclusion of the study we hope to be able to show the following as related to the anesthetic technique of apneic oxygenation:

1. Changes in pH, pCO_2 and pO_2 in arterial blood.
2. Changes in arterial-alveolar oxygen gradients as a reflection of V/Q.
3. Rate and volumes of oxygen flow into lungs from upper airways.
4. Changes in lung volumes (FRC).

G. BIBLIOGRAPHY:

1. Anthonisen, Nicholas R.: Effect of volume and volume history of the lungs on pulmonary shunt flow. Amer. J. Physiol. 207 (1): 235-238, 1964.
2. Heller, M. L., Watson, R. T., and Imredy, D. S.: Apneic oxygenation in man: Plarographic arterial oxygen tension study. Anesthesiology 25 (1): 25-30, 1964.
3. Bergman, Norman A.: Concerning sweet dreams, health, and quiet breathing. Anesthesiology 32 (4): 297-298, 1970.
4. Frumin, J. M., Epstein, R. M., and Cohen, G.: Apneic oxygenation in man. Anesthesiology 20 (6): 789-798, 1959.
5. Fujimori, Mitsugu, Virtue, R. W.: The value of oxygenation prior to induced apnea. Anesthesiology 21 (1): [illegible]

BUMED 5216/8 (REV. 6-70)

(2) NAVAL PERSONNEL
(3) MARINE CORPS

SERIAL: 5056

FROM CODE: 7171

DATE: 7 Dec. 1971

IDENTIFICATION

ORIGINATOR'S IDENTIFICATION DATA	DATE OF LETTER	DATE RECEIVED	REPLY DUE
From: NR [illegible] Calif. To: [illegible]	2 Dec. 1971	7 Dec. 1971	

NAME OF INDIVIDUAL (When applicable)	SUBJECT IDENTIFICATION CODE
H.P. MAHIN	78:bb 3900:6401

SUBJECT

Use of human volunteers in connection with a study on Apenic Oxygenation in Anesthesia; request for approval of

INSTRUCTIONS

1. Each correspondence control desk shall detach a copy of this form and use it as its control log. On the log copy, indicate internal routing of correspondence. Remove extra carbons as copies are pulled.
2. When submitting correspondence to Codes 1 and 2 for signature, submit at least the original and one copy of this form.
3. See BUMEDINST 5216.10 series for detailed procedures.

ROUTING AND CLEARANCE

ROUTING *SYMBOLS: A-Action, CL-Clearance, C-Comment, I-Information, R-Retain, SC-Separate Copy, S-Signature

TO CODE	FOR *	CONTROL DESK IN	CONTROL DESK OUT	COMMENTS BY CLEARANCE CODES (If more space is needed, use memo and indicate below "Memo attached.")	DATE	INITIAL
W71						
712	A					
10	C	12/16/71	12/16/71	Yes, I believe it is an unusual request (4C) + should have SECNAV approval	12/16/71	G H R

FOR SIGNATURE MAIL

ASSISTANT CHIEF Code						
DEPUTY CHIEF						
CHIEF OF BUREAU						

PREPARED BY (Organization Title and Code) | TELEPHONE EXTENSION

BRIEF ALL CORRESPONDENCE FOR SIGNATURE BY THE CHIEF OR DEPUTY (SUPPLY SIGNIFICANT DATA, OMIT MINOR DETAILS)

SIGNATURE (Division Director) | DATE

FOR CODE 1 OFFICE USE

RECEIVED	RETURNED

DISPOSITION

	SIGNED		PICKED UP
	MAILED		OTHER

SALUTATION:

COMMENTS:

Previous issues of this form and BUMED 5216/5 and BUMED 45-12 are obsolete.

A-27280