

Award Number: W81XWH-13-2-0022

TITLE: Evaluation of Neurophysiologic and Systematic Changes during Aeromedical Evacuation and en Route Care of Combat Casualties in a Swine Polytrauma Model

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CONTRACTING ORGANIZATION: Henry M. Jackson Foundation  
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Fort Detrick, Maryland 21702-5012

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# REPORT DOCUMENTATION PAGE

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| <b>4. TITLE AND SUBTITLE</b><br>Evaluation of Neurophysiologic and Systematic Changes during Aeromedical Evacuation and en Route Care of Combat Casualties in a Swine Polytrauma Model  |                         |                                 |   | <b>5a. CONTRACT NUMBER</b>                                   |   |
| <b>6. AUTHOR(S)</b><br>Richard McCarron, PhD<br>Anke Scultetus, MD<br><br>E-Mail: Richard.McCarron@med.navy.mil; Anke.Scultetus@med.navy.mil  |                         |                                 |   | <b>5d. PROJECT NUMBER</b><br>W81XWH-13-2-0022                |   |
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| <b>7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)</b><br>Henry M. Jackson Foundation<br>Bethesda, MD 20817-1834   |                         |                                 |   | <b>8. PERFORMING ORGANIZATION REPORT NUMBER</b>              |   |
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| <b>12. DISTRIBUTION / AVAILABILITY STATEMENT</b><br>Approved for Public Release; Distribution Unlimited   |                         |                                 |   |  |   |
| <b>13. SUPPLEMENTARY NOTES</b>  |                         |                                 |   |  |   |
| <b>14. ABSTRACT</b><br>There is a dearth of knowledge about the effects of long range aero-medical evacuation on injured organs, as well as an emerging published database suggesting clinically significant adverse effects of hypobarica on even healthy tissues. Cabin pressure is equivalent to an altitude around 8,000ft. at which inspired oxygen is sufficient to maintain blood oxygen saturation above 90% in a healthy individual. In combat casualties with multiple injuries this could however compromise oxygen delivery and result in hypoxemia. Additionally, increase in altitude with concomitant decrease in atmospheric pressure allows gas expansion in body cavities. The volume of trapped gas expands by approximately 35% from sea level to an altitude of 8,000 feet. This can expose already vulnerable patients to severe complications. In light of this, a thorough investigation of the effects of hypobarica in clinical settings simulating the most important injury patterns encountered by combat casualties is necessary to optimize treatment efficacy and safety. During the first year of this project, the Naval Medical Research Center (NMRC) designed and built a chamber that can be de-pressurized to atmospheric pressure at 8,000ft. Chamber construction has been completed and swine experiments have been initiated. The NMRC Center for Hypobaric Experimentation, Simulation and Testing (CHEST) provides a unique platform for evaluation of long-range evacuation effects on physiology and therapeutic interventions in military relevant large animal combat injury models, which may contribute to optimization of combat casualty care and evacuation guidelines. |                         |                                 |   |  |   |
| <b>15. SUBJECT TERMS</b><br>Aeromedical evacuation, en-route care, hypobaric conditions, hypobaric chamber, swine model   |                         |                                 |   |  |   |
| <b>16. SECURITY CLASSIFICATION OF:</b>  |                         |                                 | <b>17. LIMITATION OF ABSTRACT</b><br><br>UU | <b>18. NUMBER OF PAGES</b><br><br>9                          | <b>19a. NAME OF RESPONSIBLE PERSON</b><br>USAMRMC |
| <b>a. REPORT</b><br>U   | <b>b. ABSTRACT</b><br>U | <b>c. THIS PAGE</b><br>U        |   |  | <b>19b. TELEPHONE NUMBER</b> (include area code)  |

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## **INTRODUCTION:**

Rapid evacuation of combat casualties to definitive care in the United States is practice based on evidence derived from recent military conflicts and has greatly diminished morbidity and mortality among combat casualties. However, not much is known about the effects of long range aero-medical evacuation in hypobaric environments on the physiology and organ function of injured warfighters, thus potentially and unknowingly putting combat casualties at risk during evacuation. Traumatic brain injury (TBI) patients are of particular concern, since small changes in ambient conditions such as cabin pressure and temperature could potentially have detrimental effects on the already vulnerable brain. There is evidence that hypobaria as well as in-flight cabin pressure fluctuations can induce neurological symptoms in otherwise healthy persons due to altitude decompression sickness. This suggests that high altitude hypobaric conditions can have detrimental effects on pulmonary and neurologic outcome and that aero-medical conditions and/or therapeutics can be optimized to attenuate such adverse effects.

Our hypothesis is that hypobaria during simulated long-range aero-medical evacuation has adverse effects on brain blood flow and tissue oxygenation, as well as lung function in swine models of neurotrauma and polytrauma. We plan to investigate the effects of aero-medical evacuation on neurophysiology and lung function in swine models of TBI with and without hemorrhagic shock (HS) and/or ARDS (polytrauma).

## **BODY:**

There were three tasks scheduled to be completed or initiated within the first year of this grant:

### **Task 1. Build Hypobaric chamber (months 1-14):**

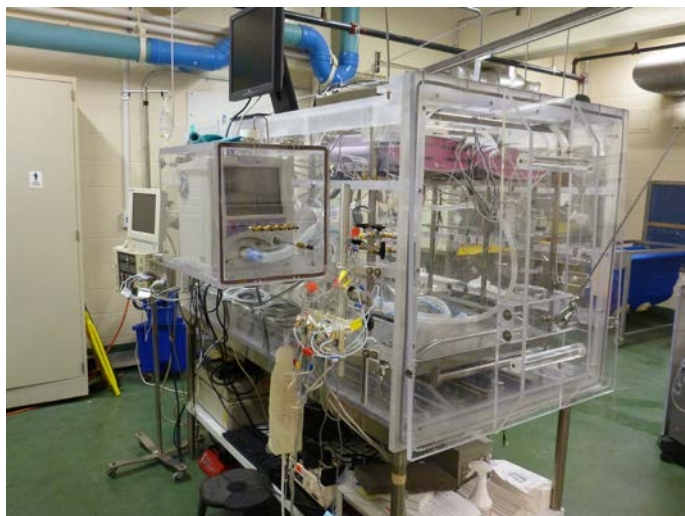
*Subtask 1. Complete engineering plans for construction (months 1-2).*

*Subtask 2. Acquire materials (months 2-4).*

*Subtask 3. Construction of chamber in machine shop at NMRC (months 5-14).*

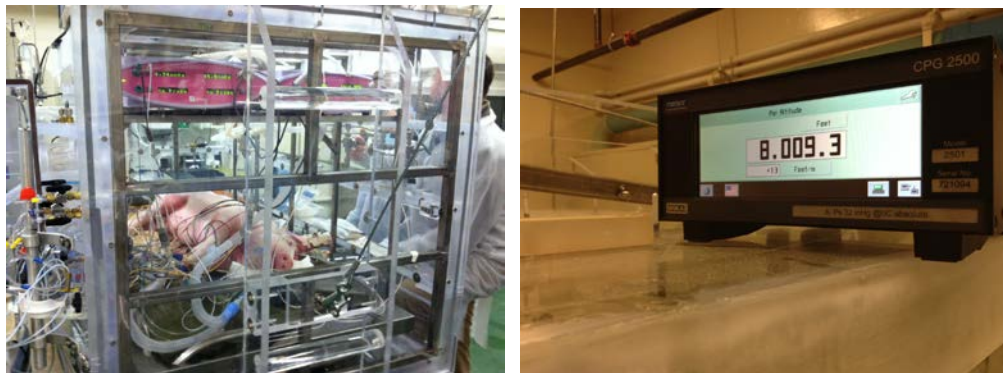
A pillar for the work to be accomplished for this grant is the design and construction of a chamber that can be de-pressurized to simulate long-range flight cabin pressures equivalent to 8,000 feet for the use of experiments in large animals. This is a unique capability within the entire military and civilian research community. Engineers at the Naval Medical Research Center experienced with the construction and maintenance of hyperbaric chambers for swine experiments to simulate deep sea dives in the Undersea Medicine Department have designed and completed construction of the hypobaric chamber for the experiments planned on this project within the first year (Fig. 1). The NMRC Center for Hypobaric Experimentation, Simulation and Testing (CHEST) provides a unique platform for evaluation of long-range evacuation effects on physiology and therapeutic interventions in military relevant large animal combat injury models, which may contribute to optimization of combat casualty care and evacuation guidelines.

Fig.1: NMRC Center for Hypobaric Experimentation, Simulation and Testing (CHEST) – Large animal hypobaric chamber.



To our knowledge, this is the first hypobaric chamber built for trauma research and extensive data collection in swine. As a result, there were several unanticipated challenges associated with pressure differentials inside and outside the chamber, all of which have been resolved. The first pilot experiment has been completed within the first year of this grant, with a successful “flight” of an anesthetized, 30 kilogram Yorkshire swine (Fig.2).

Fig.2: First anesthetized swine in the chamber at 8,000 ft altitude.



**Task 2. IACUC approval for animal study (months 1-4):**

*Subtask 1. Write IACUC protocol (month 1).*

*Subtask 2. IACUC review and approval (months 2-4).*

The IACUC protocol has been written and approved by the WRAIR/NMRC IACUC (07JAN2013) and ACURO (JAN292013) within the first month of this grant.

**Task 3. Animal experiments during normobaric conditions (months 5-28):**

*Subtask 1. Complete 72 animal experiments in Sham, TBI alone, TBI+HS, ARDS alone, TBI+ARDS and TBI+HS+ARDS groups. Animals will be randomized (months 5-28)*

*Subtask 2. Hematologic and hematologic analysis of blood samples (months 5-28).*

*Subtask 3. Necropsy, gross pathology, histopathologic analysis (months 5-28).*

During the construction of the hypobaric chamber, it became evident that physiological and neurophysiological monitoring equipment need to be permanently integrated into the chamber due to the requirement of airtight penetration for the cables. Therefore, the hypobaric chamber needs to also be used for normobaric control experiments. We do not anticipate that this required delay in starting animal work will be of consequence for the timely completion of all animal work associated with this grant.

**Task 4. Animal experiments during hypobaric conditions (months 15-39):**

*Subtask 1. Complete 10 pilot animals to test hypobaric chamber and animal set up for monitoring within the chamber (months 15-16).*

*Subtask 2. Complete 72 animal experiments in Sham, TBI alone, TBI+HS, ARDS alone, TBI+ARDS and TBI+HS+ARDS groups. Animals will be randomized (months 17-39)*

*Subtask 3. Hematologic and hematologic analysis of blood samples (months 17-39).*

*Subtask 4. Necropsy, gross pathology, histopathologic analysis (months 17-39).*

The construction of the hypobaric chamber has been slightly ahead of schedule, and pilot animals to the chamber and monitoring equipment has been initiated in month 12 of the grant.

**KEY RESEARCH ACCOMPLISHMENTS:**

- IACUC and ACURO animal use protocol approval (Protocol # 13-OUMD-02LS)
- Design and construction of a hypobaric chamber that can be de-pressurized to atmospheric pressure at 8,000 ft, and that can collect physiologic and neurophysiologic data in anesthetized large animals.
- Initiation of pilot experiments to test chamber in a live, anesthetized animal.

**REPORTABLE OUTCOMES:**

None.

**CONCLUSION:**

The hypobaric chamber for simulating swine experiment during long-range aeromedical evacuation flights built for this grant provides a unique platform for evaluation of long-range evacuation effects on physiology and therapeutic interventions in military relevant large animal combat injury models. The creation of the NMRC Center for Hypobaric Experimentation, Simulation and Testing (CHEST) may contribute to optimization of combat casualty care and evacuation guidelines.

**REFERENCES:**

None.

**APPENDICES:**

1. WRAIR/NMRC IACUC approval of animal use protocol.
2. ACURO approval of animal use protocol.

**SUPPORTING DATA:**

None.



DEPARTMENT OF THE ARMY  
WALTER REED ARMY INSTITUTE OF RESEARCH  
503 ROBERT GRANT AVENUE  
SILVER SPRING, MD 20910-7500

REPLY TO  
ATTENTION OF

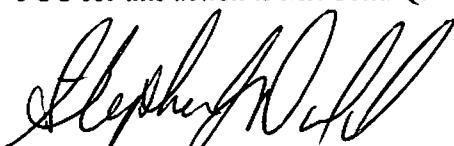
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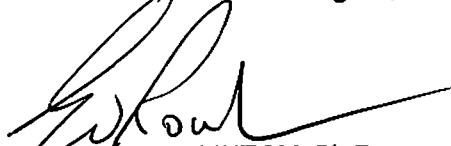
7 January 2013

MEMORANDUM FOR Richard M. McCarron, Ph.D., NeuroTrauma Department, Operational & Undersea Medicine Directorate, Naval Medical Research Center, 503 Robert Grant Avenue, Silver Spring, MD 20910-7500

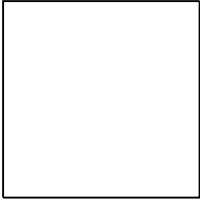
SUBJECT: Protocol Approval, WRAIR/NMRC Institutional Animal Care and Use Committee

1. Protocol 13-OUMD-02LS, "Evaluation of neurophysiologic, pulmonary and systemic changes during aero-medical evacuation and enroute care of combat casualties in a swine polytrauma model (*Sus scrofa domestica*)" has been reviewed by Designated Member Review and approved IAW WRAIR Policy Letter 11-31, "Institutional Animal Care and Use Committee and Protocol Review" for 168 Yorkshire Swine and will expire 6 January 2016.
2. You are required to submit an Annual Review Form each fiscal year to the IACUC Office. Protocols may be subject to suspension if the PI does not comply in providing the Annual Review Form.
3. The PI is required to submit an amendment requesting a change of PI if he or she is being transferred or leaves the Institute for any reason. Active protocols must be transferred to a new PI prior to the departure of the original PI. It is recommended that the original PI submit an Annual Review Form covering any work done in the current fiscal year prior to the transfer.
4. Before acquiring animals, a protocol-planning meeting is required. The protocol-planning meeting ensures issues such as animal housing and monitoring, acquisition of special supplies/equipment, occupational health, and safety is addressed. Such meetings should include the PIs, associate investigators and VSP personnel. Please contact the appropriate VSP veterinarian or NCOIC to coordinate the meeting.
5. POC for this action is Mr. Seitu Q. Khafre, at 301-319-9051, or the undersigned, 301-319-9299.

  
STEPHEN J. DALAL, LTC, VC  
DESIGNATED MEMBER  
WRAIR/NMRC Institutional  
Animal Care and Use Committee

  
EDGAR D. ROWTON, Ph.D.  
Chair, WRAIR/NMRC Institutional  
Animal Care and Use Committee

CF:  
C, LAMB  
Consulting Vet, LTC Stephens-DeValle



DEPARTMENT OF THE ARMY  
US ARMY MEDICAL RESEARCH AND MATERIEL COMMAND  
504 SCOTT STREET  
FORT DETRICK, MD 21702-5012

January 29, 2013

Director, Office of Research Protections  
Animal Care and Use Review Office

Subject: Review of USAMRMC Proposal Number PT110638, Award Number W81XWH-13-2-0022 entitled, "Evaluation of Neurophysiologic and Systematic Changes During Aeromedical Evacuation and en Route Care of Combat Casualties in a Swine Polytrauma"

Principal Investigator Richard McCarron  
Naval Medical Research Center (NMRC), Silver Spring  
Silver Spring, MD

Dear Dr. McCarron:

Reference: (a) DOD Instruction 3216.01, "Use of Animals in DOD Programs"  
(b) US Army Regulation 40-33, "The Care and Use of Laboratory Animals in DOD Programs"  
(c) Animal Welfare Regulations (CFR Title 9, Chapter 1, Subchapter A, Parts 1-3)

In accordance with the above references, the review of protocol PT110638 entitled, "Evaluation of Neurophysiologic, Pulmonary and Systemic Changes During Aeromedical Evacuation and en Route Care of Combat Casualties in a Swine Polytrauma model (sus Scrofa domestica)," IACUC protocol number 13-OUMD-02LS, by a DOD laboratory animal veterinarian is accepted and therefore approved by the USAMRMC Animal Care and Use Review Office (ACURO) for the use of swine and will remain so until its modification, expiration or cancellation. This protocol was approved by the Walter Reed Army Institute of Research (WRAIR), Silver Spring IACUC.

When updates or changes occur, documentation of the following actions or events must be forwarded immediately to ACURO:

- IACUC-approved modifications, suspensions, and triennial reviews of the protocol (All amendments or modifications to previously authorized animal studies must be reviewed and approved by the ACURO prior to initiation.)
- USDA annual program/facility inspection reports
- Reports to OLAW involving this protocol regarding
  - a. any serious or continuing noncompliance with the PHS Policy;
  - b. any serious deviation from the provisions of the Guide for the Care and Use of Laboratory Animals; or
  - c. any suspension of this activity by the IACUC



- USDA or OLAW regulatory noncompliance evaluations of the animal facility or program
- AAALAC, International status change (gain or loss of accreditation only)

Throughout the life of the award, the awardee is required to submit animal usage data for inclusion in the DOD Annual Report on Animal Use. Please ensure that the following animal usage information is maintained for submission:

- Species used (must be approved by this office)
- Number of each species used
- USDA Pain Category for all animals used

For further assistance, please contact the Director, Animal Care and Use Review Office at (301) 619-2283, FAX (301) 619-4165, or via e-mail: [acuro@amedd.army.mil](mailto:acuro@amedd.army.mil).

***NOTE: Do not construe this correspondence as approval for any contract funding. Only the Contracting Officer or Grant Officer can authorize expenditure of funds. It is recommended you contact the appropriate Contract Specialist or Contracting Officer regarding the expenditure of funds for your project.***

Sincerely,



James Sheets, DVM, DACLAM  
Colonel, US Army  
Director, Animal Care and Use  
Review Office

Copies Furnished:

- Mr. Ayi Ayayi, US Army Medical Research Acquisition Activity
- Dr. Bao-Han Christie Vu, Congressionally Directed Medical Research Program
- Mr. Seitu Q. Khafre, Walter Reed Army Institute of Research, Silver Spring
- Ms. Eileen McDaniel, Naval Medical Research Center, Silver Spring
- Ms. Marianne Spevak, Henry M. Jackson Foundation for the Advancement of Military Medicine
- Dr. Inna Williams, Congressionally Directed Medical Research Program