AWARD NUMBER: CDMRPL-16-0-DM167040

TITLE: Preclinical Evaluation of the Effects of Aeromedical Evacuation on Military-Relevant Casualties

PRINCIPAL INVESTIGATOR: Dr. Anke H. Scultetus

CONTRACTING ORGANIZATION: Naval Medical Research Center
Silver Spring, MD 20910

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PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

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REPORT DOCUMENTATION PAGE

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1. REPORT DATE	**2. REPORT TYPE**	**3. DATES COVERED**
OCTOBER 2018	ANNUAL	1 Oct 2017 - 30 Sep 2018

4. TITLE AND SUBTITLE

Preclinical Evaluation of the Effects of Aeromedical Evacuation on Military-Relevant Casualties

5a. CONTRACT NUMBER

5b. GRANT NUMBER
CDMRPL-16-0-DM167040

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Dr. Anke Scultetus

E-Mail: anke.h.scultetus2.civ@mail.mil

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Naval Medical Research Center
503 Robert Grant Avenue

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

Current practice in Operation Enduring Freedom commonly includes transport of the critically injured patient to the Continental United States (CONUS) soon after stabilization and initial surgery. In general, service members can be returned to the US medical treatment facility in five-to-seven days. Aeromedical transport is associated with obvious concerns that include hypobaria, hypoxemia, air trapped within a body cavity, vibration, and hypothermia. Current guidelines for critical care air transport teams (CCATT) note that basic physiology parameters during transport are to be supported; to include adequate oxygen saturation, ventilation, blood pressure etc. However, these parameters may be difficult to achieve. The impact of hypobaria on the transport of critically ill patients is unknown. Applying resuscitation guidelines for trauma developed over decades for ground-based scenarios to aeromedical transport is simply based on expert opinion.
This grant incorporates three projects that address specific operational issues regarding optimization of aeromedical evacuation standards. In animal models of combat trauma, we will address the effects of timing, altitude, and oxygen supplementation during aeromedical evacuation.

15. SUBJECT TERMS

NONE LISTED

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON**
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			USAMRMC
Unclassified	Unclassified	Unclassified	Unclassified	19	**19b. TELEPHONE NUMBER** *(include area code)*

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1. **INTRODUCTION:** *Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.*

Current practice in Operation Enduring Freedom commonly includes transport of the critically injured patient to the Continental United States (CONUS) soon after stabilization and initial surgery. In general, service members can be returned to the US medical treatment facility in five-to-seven days. Aeromedical transport is associated with obvious concerns that include hypobaria, hypoxemia, air trapped within a body cavity, vibration, and hypothermia. Current guidelines for critical care air transport teams (CCATT) note that basic physiology parameters during transport are to be supported; to include adequate oxygen saturation, ventilation, blood pressure etc. However, these parameters may be difficult to achieve. The impact of hypobaria on the transport of critically ill patients is unknown. Applying resuscitation guidelines for trauma developed over decades for ground-based scenarios to aeromedical transport is simply based on expert opinion. This grant incorporates three projects that address specific operational issues regarding optimization of aeromedical evacuation standards. In animal models of combat trauma, we will address the effects of timing, altitude, and oxygen supplementation during aeromedical evacuation.

2. **KEYWORDS:** *Provide a brief list of keywords (limit to 20 words).*

Traumatic brain injury; hemorrhagic shock; aeromedical evacuation; oxygenation, altitude; timing of evacuation

3. **ACCOMPLISHMENTS:** *The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction.*

What were the major goals of the project?
List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

	Timeline	Method	Status
Specific Aim 1: Evaluation of the timing of aeromedical evacuation in rat and swine models of TBI and polytrauma	Months		
Major Task 1: IACUC/ACURO approval	1-3	Writing	complete
Major Task 2: Rat blast/AE timing experiments	4-20	Animal experiment	ongoing
Major Task 3: Swine TBI/polytrauma AE timing experiments	21-32	Animal experiment	
Major Task 4: Data analysis/manuscript/final report	33-36	Statistics/ writing	

	Timeline	Method	Status
Specific Aim 2: The effects of oxygen supplementation during aero-medical evacuation on brain oxygenation in swine with fluid-percussion (FP) - traumatic brain injury (TBI)			
Major Task 1: IACUC/ACURO approval	6-9	Writing	Complete
Major Task 2: Swine supplemental O_2 /AE experiments	10-38	Animal experiment	Ongoing
Major Task 3: Data analysis/manuscript/final report	39-42	Statistics/ writing	
Specific Aim 3: Physiological consequences of 4,000 and 8,000 ft. altitude aeromedical evacuation on swine with traumatic brain injury and hemorrhagic shock			
Major Task 1: IACUC/ACURO approval	36-39	Writing	
Major Task 2: Swine AE/altitude experiments	40-57	Animal experiment	
Major Task 3: Data analysis/manuscript/final report	57-60	Statistics/ writing	

What was accomplished under these goals?

For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

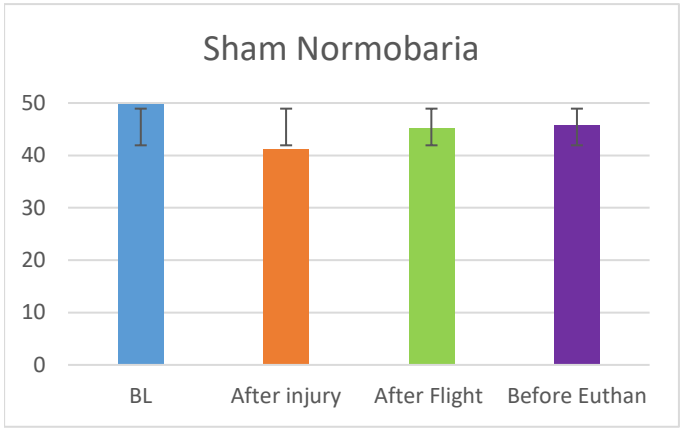
Specific Aim 1: Evaluation of the timing of aeromedical evacuation in rat and swine models of TBI and polytrauma:

We are currently working on the first experimental phase where we exposed rats to blast overpressure (3 consecutive blasts at 110kPa on Day 1) and then delayed the simulated 6-hour flight (altitude at 8000ft cabin pressure) for 2 days, 7 days, and 14 days post blast in order to assess any changes on motor function and physiology after both the blast TBI and flight. The euthanasia time point for all groups has been 8 days after flight and we have been collecting brain, heart, lung, liver, intstine, and kidney tissue for molecular analyses as well as plasma from blood for cytokine expression and CBC. We have also sent the remaining tissues to be processed and stained (H&E) for histopathological analysis. At this time, we have completed the 7 day flight (7 day flight post blast exposure) cohort and have analyzed behavioral and cytokine data (see attached graphs). Contrary to our hypotheses, we have not found any significant deficits in motor behavior among the animals exposed to blast and hypobaric flight conditions, as behavioral performance on the rotarod test was consistent across all groups. The cytokine expression was analyzed from

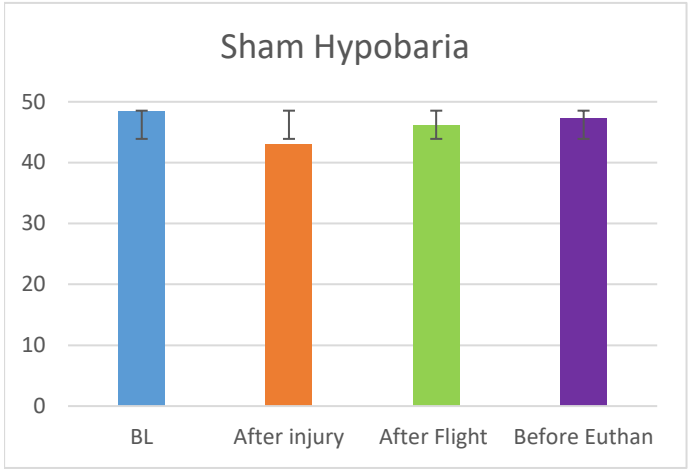
plasma from all groups and samples were processed with a commercial Luminex (Multiplex) kit that probed for a panel of various cytokines/chemokines. There was much variability among the cytokine results, but we have seen a trend of an increase in the IL-18, MCP-1, and RANTES chemokines in the animals exposed to blast and hypobaria. We are currently waiting for histopathology data to determine if significant organ damage occurred after the 7-day delayed flight and blast TBI. We are also close to finishing the other cohorts of animals that experience the 14-Day flight after blast exposure. We are currently conducting more data and histological analyses for these other cohorts.

Figure 1: Motor behavioral performance on the rotarod test in the 7-Day flight cohort

A.



B.



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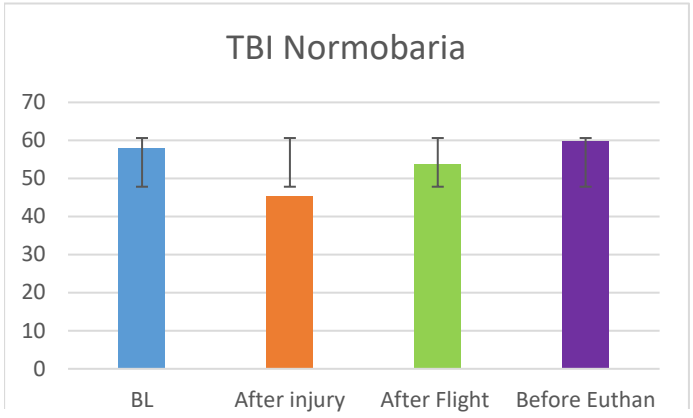
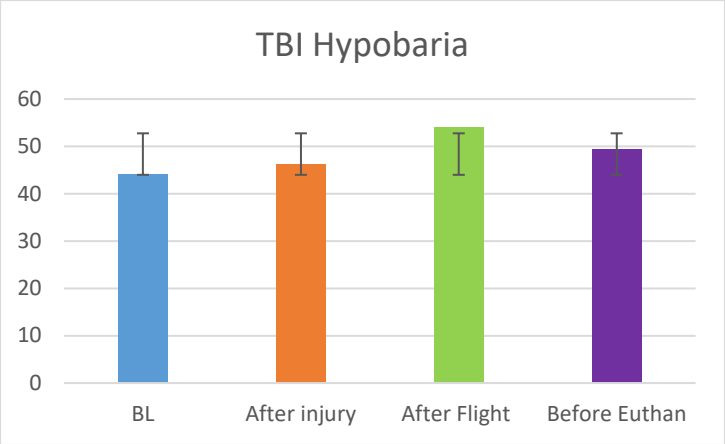
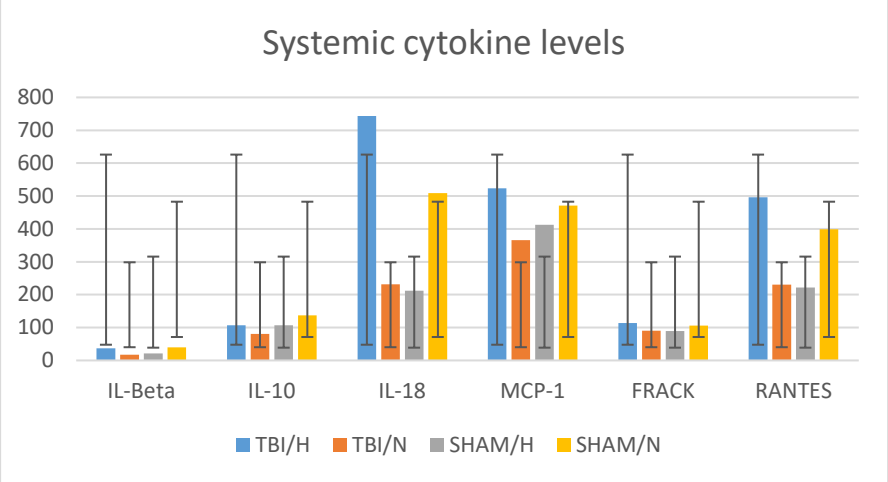


D.



NOTE: All data after flight and injury are shown as a percentage change from the baseline balance scores on the rotarod. Significance level is 0.05. No significant differences in scores were observed across groups at any of the time points after baseline, suggesting that blast TBI and hypobaria exposure may not be influencing motor performance as much as predicted.

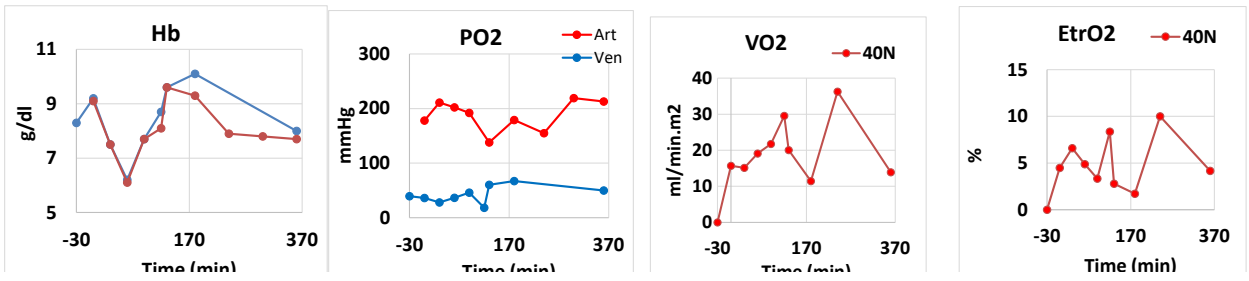
Figure 2: Cytokine/Chemokine panel assessed across all groups after blast TBI and flight
A.



NOTE: Given the large error bars of variability, no significant differences in cytokine levels were found, but a trend of increased IL-18, MCP-1, and RANTES can be seen in the control and blast TBI and hypobaria groups. Significance is also at the 0.05 level.

Specific Aim 2: The effects of oxygen supplementation during aero-medical evacuation on brain oxygenation in swine with fluid-percussion (FP) - traumatic brain injury (TBI):
Specific objectives: Establish an appropriate experimental setting for performing the experiments related to this oxygen supplementation study during aeromedical evacuation. Due to the complexity of the experimental setting it was necessary to conduct additional testing, validation and modification of the devices (i.e. to ensure that all devices (physiological monitoring devices, drilling equipment for the skull, hypobaric chamber) were in high standard working mode). Similarly technical personnel needed to be trained on each phases of the procedure before being fully proficient to run the whole procedure on animals. This was necessary for the acquisition of quality experimental data.
Major activities: The current hypobaric set up had to be modified to accommodate the proposed work: Specific instrumentations have been build, set up and piping oxygen and air in the hypobaric chamber to allow for adjustment of oxygen delivery, calibrating the ventilator for the appropriate oxygen level to be delivered, testing this setting under hypobaric conditions, modifying the hypobaric chamber to allow connection for new physiologic monitoring such as introduction of the cable for intracranial pressure (ICP) monitoring, and lead wire for hemodynamic monitoring. Practice for the personnel on surgical procedures, monitoring and observation of the animal was also conducted. Pilot animals have been used to verify and adjust some of the methods for constant force during the traumatic brain injury (TBI), to monitor and compare ICP values using two different devices (Coleman and Raumedic), to validate the proper anesthesia regimen while changing from isoflurane to TIVA in order to transport the animal to the hypobaric chamber. These measures were necessary to optimize materiel and personnel resources available for the specifics of this grant. Animal work on the experimental study has been initiated with various levels of oxygen being delivered to the animal.
Significant results: Typical data patterns are illustrated below. For a 40% oxygenation level at normobaria following injury: Under lowered hemoglobin (Hb) but sufficient arterial PO2 supply (40%), the oxygen consumption (VO2) and extraction (EtrO2) tend to decrease after the connection of the animal to the chamber oxygen (Fig 1). For a 74% oxygenation level at normobaria following injury: Under lowered hemoglobin (Hb) but sufficient arterial PO2 supply (74%), the oxygen consumption (VO2) and extraction (EtrO2) tend to remain stable after the connection of the animal to the chamber oxygen (Fig 2).
Other parameters such as mean arterial pressure (MAP) and Heart Rate (HR) are restored after the injury by the resuscitation regimen. These parameters remained stable during transport. Experiments under hypobaric conditions have not been conducted for the full length of the protocol.

Conclusion: We have designed a model that will allow us to compare the effect of various levels of oxygenation in a polytraumatized animals under both normobaric and hypobaric conditions. During the coming year, data will be generated for each of the experimental groups as indicated in the table.



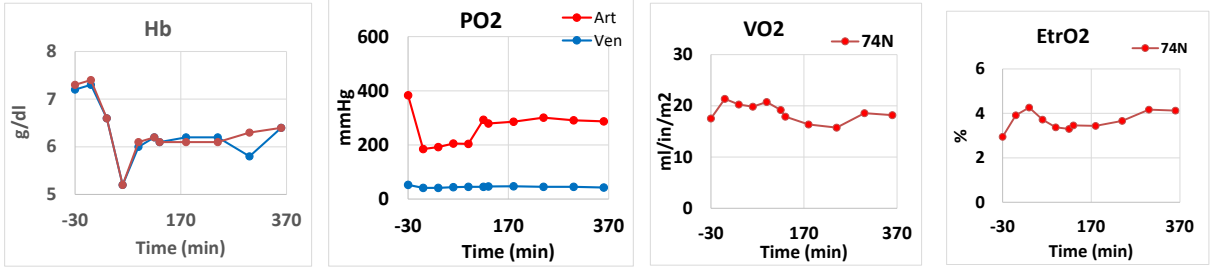


Fig 2: Normobaria at 74% oxygenation

Code	Experiment	O2 at sea level	O2 in flight
Pilot			Surface Equivale
SHAM	No-injury	40%	29%
21N	21%FiO2	21%	
29N	29%FiO2	29%	21%
48N	40%FiO2	40%	29%
54N	54%FiO2	54%	40%
74N	74%FiO2	74%	54%
100N	100%FiO2	100%	74%

Table: Experimental groups

What opportunities for training and professional development has the project provided?
If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. "Training" activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. "Professional development" activities result in increased knowledge or skill in one's area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.

This project so far provided several one-on-one training activities for new employees who will work as junior scientists or research assistants on this project. Through literature search and regular discussion groups within our team we were able to significantly increase their knowledge platform in regards to battlefield care, general physiology and flight physiology.

How were the results disseminated to communities of interest?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

Nothing to report.

What do you plan to do during the next reporting period to accomplish the goals?
If this is the final report, state "Nothing to Report."

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

Specific Aim 1: Evaluation of the timing of aeromedical evacuation in rat and swine models of TBI and polytrauma:
We plan to continue to carry out all experiments as planned from now until the next reporting period. We will conduct several molecular assays on tissues in addition to reviewing histological data in order to determine the physiological effects of the various flight times post blast TBI.

Specific Aim 2: The effects of oxygen supplementation during aero-medical evacuation on brain oxygenation in swine with fluid-percussion (FP) - traumatic brain injury (TBI):
The hypobaric chamber has been transferred to a different location due to construction projects in the building and requires to be retested for its full operational use. This extra step was not anticipated and will need to be accomplished first. Experimental animal groups will then be completed as described in the proposal for the escalation from 29% to 100% oxygenation at normo-and hypobaria. Data will be acquired at regular intervals including hemodynamics (MAP, HR, cardiac output), oxygenation (O2, EtCO2,PtO2), brain pressure (ICP), blood work and histopathology. Animals will be distributed randomly to groups therefore we do not expectt to complete any blocks of groups; however if the animal number per group permits, interim statistical analysis will be performed.

4. **IMPACT:** D*escribe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:*

What was the impact on the development of the principal discipline(s) of the project?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

Nothing to report.

What was the impact on other disciplines?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

Nothing to report.

What was the impact on technology transfer?
If there is nothing significant to report during this reporting period, state "Nothing to Report."
Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:

- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

This project will likely have an impact on revisiting current practices in patient transport and aeromedical evacuation, as well as standard operating procedures during aeromedical transport.

What was the impact on society beyond science and technology?
If there is nothing significant to report during this reporting period, state "Nothing to Report."
Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:

- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

Nothing to Report.

5. **CHANGES/PROBLEMS:** *The PD/PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:*

Nothing to report.

Changes in approach and reasons for change
Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.

N/A

Actual or anticipated problems or delays and actions or plans to resolve them
Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

Nothing to report.

Changes that had a significant impact on expenditures
Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

There were no changes that impacted expenditure during this reporting period.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents
Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

Significant changes in use or care of human subjects

N/A

Significant changes in use or care of vertebrate animals

N/A

Significant changes in use of biohazards and/or select agents

N/A

6. **PRODUCTS:** *List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."*

- **Publications, conference papers, and presentations**
  Report only the major publication(s) resulting from the work under this award.

Francoise Arnaud, Richard McCarron, Carl Goforth, Anke Scultetus. Model for defining an optimal O2 level during flight. Military Health Sciences Research Symposium (MHSRS) 20-23 Aug 2018, Orlando FL.

Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to report.

Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to report.

Other publications, conference papers and presentations. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.*

Nothing to report.

- **Website(s) or other Internet site(s)**

List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Nothing to report.

- **Technologies or techniques**
  Identify technologies or techniques that resulted from the research activities. Describe the technologies or techniques were shared.

Nothing to report.

- **Inventions, patent applications, and/or licenses**
  Identify inventions, patent applications with date, and/or licenses that have resulted from the research. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

Nothing to report.

- *outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment and /or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:*
  - *data or databases;*
  - *physical collections;*
  - *audio or video products;*
  - *software;*
  - *models;*
  - *educational aids or curricula;*
  - *instruments or equipment;*
  - *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
  - *clinical interventions;*

- *new business creation; and*
- *other.*

Nothing to report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change".

Personnel	**Role**	**Person month worked**
Dr. Anke Scultetus	PI	1
Col Debra Malone	AI	1
Noemy Carballo	Senior Research Assistant: animal	4
Dr. Francoise Arnaud	Scientist: project management	2
Dr. Yaron Dayani	Research Associate: data analysis	4
Meghan Patterson	Research Assistant: animal, data	4
Jordan Hubbell	Research Assistant: animal, data	4
Joel Duberstein	Research Assistant: animal, data	4
Michael Hammett	Research Assistant: hematology	2
William Porter	Chamber Operator	2
Andrea White	Research Assistant: animal, data	4
Fang Zhou Yang	Research Assistant: animal, data	4
Alexander Connor	Research Assistant: animal, data	4
Dr. Ye Chen	Scientist: molecular biology	2
Dr. Melissa Mehalick	Research Associate: Data Analaysis	4

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

Change of PI from Dr. Richard McCarron to Dr. Anke Scultetus.

What other organizations were involved as partners?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.

Provide the following information for each partnership:
Organization Name:
Location of Organization: (if foreign location list country)
Partner's contribution to the project (identify one or more)

- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner's facilities for project activities);*
- *Collaboration (e.g., partner's staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); and*
- *Other.*

Nothing to report.

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: *For collaborative awards, independent reports are required from BOTH the Initiating Principal Investigator (PI) and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to* ***https://ers.amedd.army.mil*** *for each unique award.*

QUAD CHARTS: *If applicable, the Quad Chart (available on https://www.usamraa.army.mil) should be updated and submitted with attachments.*

Evaluation of the Timing of Aeromedical Evacuation in Rat and Swine Models of TBI and Polytrauma

Joint En Route Care Award - Intramural
Log Number DM167040 - Project 1

PI: Dr. Anke Scultetus **Site-PI:** Dr. Anke H. Scultetus, Dr. Stephen T. Ahlers **Org:** NMRC/USUHS **Award Amount:** $1,176,000

Study/Product Aim(s)

- This proposal aims to clarify appropriate timing for altitude transport based on whole animal physiology, regional organ perfusion, inflammatory markers and tissue damage.
- We hypothesize that long range aeromedical transport of trauma victims effects specific organ blood flow, inflammation and histological markers of tissue damage and that these endpoints can be modified by the timing of altitude transport.

Approach

We propose to investigate the relationship between standard versus delayed aeromedical evacuation and possible influences on patient outcome in a realistic combat casualty care, evacuation and definitive care study in rats and swine. Rats will receive one 120 kPa blast; swine will receive TBI or ARDS. Animals will undergo aeromedical evacuation on day 3 after injury (standard), or they will be on a delayed transport schedule of 7,10 or 14 days.

Rapid evacuation of combat casualties to CONUS is current standard. However, our lab showed that hypobaria reduces brain tissue oxygenation in TBI swine. This study will evaluate the effects of the timing of evacuation.

Timeline and Total Cost

Activities / FY	17	18	19	20	21
IACUC/ACURO approval					
Rat blast/AE timing experiments					
Swine TBI/polytrauma AE timing experiments					
Data analysis, final report, manuscript preparation					
Estimated Total Budget ($K)	181	179	200	200	416

Goals/Milestones
FY17 Goals
X IACUC/ACURO protocol written, submitted and approved
FY18 Goals
X Begin rat blast experiments
□ Complete rat blast experiments
FY19 Goals
□ Initiate swine TBI experiments
□ Initiate swine ARDS experiments
□ Data analysis rat study
FY20 Goals
□ Continue swine experiments
FY21 Goals
□ Complete swine experiments
□ Data analysis swine study
□ Manuscript preparation and Final study report
Comments/Challenges/Issues/Concerns: None
Budget Expenditure to Date: $360K

Updated:24OCT2018

The Effects of Oxygen Supplementation During Aeromedical Evacuation on Brain Oxygenation in Swine with Fluid-Percussion (FP) - Traumatic Brain Injury (TBI)

Joint En Route Care Award – Intramural
Log Number DM167040 – Project 2

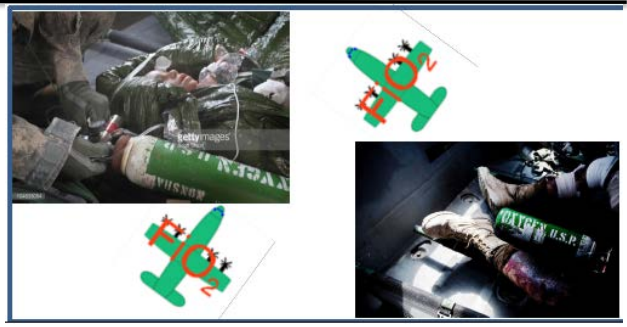
PI: Dr. Anke Scultetus **Site-PI:** Dr. Françoise Arnaud, Dr. Richard Mahon **Org:** NMRC/USUHS **Award Amount:** $577,610

Study/Product Aim(s)

- We hypothesize that hypobaria during simulated long range aero-medical evacuation has adverse effects on brain blood flow, lung function and tissue oxygenation in neurotrauma and polytrauma patients.
- In a swine model, we plan to test the hypothesis that adapted supplementation with oxygen will be beneficial to the wounded during hypobaric aero-medical evacuation.

Approach

In a polytrauma swine model combining traumatic brain injury (TBI) and hemorrhage (HS), animal physiology, and metabolic, immunologic and histologic markers of injury will be evaluated at three supplemental oxygen levels (FiO_2 of 30, 50 and 100%) during simulated altitude transport at 8,000 ft., 2 hours after injury. In flight conditions will be reproduced in a hypobaric chamber at NMRC. A total of 62 swine are needed to conduct this research.



Severely wounded are often aero evacuated with 100% oxygen supplementation. The benefit of this strategy to brain and organ function is unknown. This study evaluates 3 levels of oxygen supplementation (30, 50 and 100%) particularly on tissue oxygenation using a pre-clinical polytrauma swine model.

Timeline and Total Cost

Activities FY	17	18	19	20	21
IACUC/ACURO approval					
Swine supplemental O2 /AE experiments					
Data analysis, final report, manuscript preparation					
Estimated Total Budget ($K)	73	288	217		

Goals/Milestones:
FY17 Goal – IACUC/ACURO protocol approval
x Write and submit protocol - Get approval
X Initiate supplemental O_2 /Aero-Evacuation experiments
FY18 Goals – Swine supplemental O2 /Aero-Evacuation experiments
X Finalize Normo and Hypo settings
□ Complete oxygen supplement under normo and hypobaria
X Collect physiology and laboratory data
□ Start analyzing data
FY19 Goal – Complete project
□ Data analysis
□ Write report
□ Write – Submit manuscripts
Comments/Challenges/Issues/Concerns: None
Budget Expenditure to Date: $361K

Updated: 24OCT2018

Physiological Consequences of 4,000 and 8,000 ft. Altitude Aeromedical Evacuation on Swine with Traumatic Brain Injury and Hemorrhagic Shock

Joint En Route Care Award – Intramural
Log Number DM167040 – Project 3

PI: Dr. Anke Scultetus **Site-PI:** Col Debra Malone, MC, USAF, Dr. Anke H. Scultetus **Org:** NMRC/USUHS **Award Amount:** $919,589

Study/Product Aim(s)

- Determine if there are differences in the neurologic, cardiac, and pulmonary effects of a 4 h transport at 4,000 ft. vs. 8,000 ft. on casualties with TBI or TBI + hemorrhagic shock (HS).
- Determine if the type and severity of the injury (TBI or TBI + HS) is affected by altitude.

Approach

Animals will undergo TBI, TBI + HS, or Sham (no injury) and, after a 90 min stabilization period, will be exposed to one of three simulated transport altitudes (0, 4,000 or 8,000 ft.) for 4 h using a hypobaric chamber. TBI will be a fluid percussion injury of moderate severity (3.5 atm.) to allow comparison with previous studies; and HS will be induced by loss of 40% of blood volume.

US Navy combat nurse Lt. Cdr. Eric Gryn tends to a critically injured civilian en route to hospital. The hypobaric chamber at the Center for Hypobaric Experimentation, Simulation and Testing (CHEST) will simulate such transport in swine. It has been successfully used for two swine studies in 2016.

Timeline and Total Cost

Activities / FY	17	18	19	20	21
IACUC/ACURO approval					
Swine Aeromedical Evacuation / Altitude experiments					
Data analysis, final report, manuscript preparation					
Estimated Total Budget ($K)			287	299	334

Goals/Milestones:
FY19 Goal – IACUC/ACURO approval and begin air evac altitude experiments
- IACUC/ACURO protocol written, submitted and approved
- Pilot animals (N = 5) for technique and system verification
- Begin In-life experiments (N = 72)

FY20 Goals – Complete air evac altitude experiments
- Complete In-life experiments (N = 72)
- Batched biosamples analyzed and Histopathology
- Final database (Cleaned and locked)
- Statistical Analysis

FY21 Goal – Publication
- Manuscript preparation and submission

Comments/Challenges/Issues/Concerns: None
Budget Expenditure to Date: $0K

Updated: 24OCT2018

9. APPENDICES: *Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.*