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TITLE: Effects of Burn Injuries on Thermoregulatory and Cardiovascular Responses in Soldiers: Implications for the Standards of Medical Fitness

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14. ABSTRACT The aim of this study was to investigate whether the absolute effective body surface area (BSA) or the %BSA burned best predicts the core temperature response to exercise in the heat. Sixteen healthy non-burned individuals [8 large (LG) and 8 small (SM)] were recruited. On separate occasions, subjects cycled at ~100 W for 1 h in a 39°C, 20% relative humidity environment with a simulated burn injury of 0% or 40% total BSA. A simulated 40% burn injury reduced the effective BSA to 1.35±0.05 m ² and 1.01±0.07 m ² in LG and SM groups, respectively. Greater elevations in core temperature were observed in SM, irrespective of condition. For both groups, the elevation in core temperature was exacerbated by the 40% simulated burn (P<0.01), yet the magnitude of the increase in core temperature from 0% to 40% simulated burn was not different between groups (P=0.37). Despite the same 40%BSA burned, smaller individuals showed an ~0.75 °C greater elevation in core temperature during exercise. In exercise-based rehabilitation or physically demanding occupational settings, activities performed at the same absolute intensity will place burn survivors of smaller body size, but with the same %BSA burned, at greater risk for hyperthermia.					
15. SUBJECT TERMS Army's Standards of Medical Fitness; burn injury; thermoregulation; sweating; heat dissipation; environmental temperature; body surface area burned; donor site					
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1. INTRODUCTION

The U.S. Army's Standards of Medical Fitness pertaining to a prior burn injury is based upon the findings of only three studies, from a total of 9 subjects with burns of >40% body surface area (BSA; N=4, 3, and 2), and report contradictory findings. Equally low number of subjects were assessed in individuals with <40% BSA burned in those studies. Notably, we know nothing about the interactive effects of differing workload requirements (e.g., metabolic heat generation associated with military service) and the environmental conditions soldiers often operate in on the safety and well-being of a soldier with a prior burn injury. Further, we know nothing about the effects of differing body sizes, location of burn injury, and/or how a soldier's uniform/body armor may affect thermoregulatory and cardiovascular responses during military operations of a soldier with a burn injury. Clearly, there is insufficient information to make conclusions regarding the potential detrimental effects of a prior burn injury at the level necessary to include such recommendations in the Standards of Medical Fitness. The proposed work will provide clear and scientifically-supported guidelines that will culminate in recommendations for a revision of the US Army's Standards of Medical Fitness for burn injuries to more accurately predict the consequences of the injury on the safety and wellbeing of the burned soldier. This information will also have direct impact on the accession/retention of the burned soldier, potentially allowing highly trained, but burned, soldiers to remain in service and thereby realizing cost savings to the Army that would otherwise be spent on training replacements. Finally, the obtained information will benefit the civilian burn community, and those who treat such individuals, through specific recommendations that are dictated in part by the activity level and/or environmental conditions such individuals participate in, with a goal of mitigating the risk of heat-related injuries in this population.

2. KEYWORDS

Army's Standards of Medical Fitness; burn injury; soldier; thermoregulation; sweating; heat dissipation; exercise; metabolic heat generation; environmental climate; temperature; humidity; body surface area burned; donor site; fitness.

3. ACCOMPLISHMENTS

What were the major goals of the project: For year 2 of this project (October 1, 2016 – September 30, 2017) the Statement of Work indicates that we will complete data collection for protocols 1A and 1B and will reduce those data such that they could be disseminated to the scientific community (see last year's annual progress report for modification of the timing of completion for protocol 1B). We also proposed to initiate data collection for protocols 2A and 2C. Protocol 2A evaluates the effect of ambient temperature of individuals exercising in thermoneutral and hyperthermic environments, with simulated burns covering 0, 20%, 40%, and 60% of their body surface area. We would like to note that to complete this battery of tests each subject visits the laboratory on 9 occasions. Protocol 2C assesses the relationship between one's maximal evaporative capacity and body surface area burned. For this protocol, subjects exercise at a fixed workload, having simulated burns covering 0, 20%, 40%, and 60% of their body surface area, which is followed by escalating humidity to identify the relative humidity at which core temperature inflection point occurs. To complete this protocol, subjects visit the laboratory on 5 occasions. Finally, we also proposed that we will initiate data collection in individual with burn injuries, addressing objectives outlined in Aims 1B, 2D, and 4.

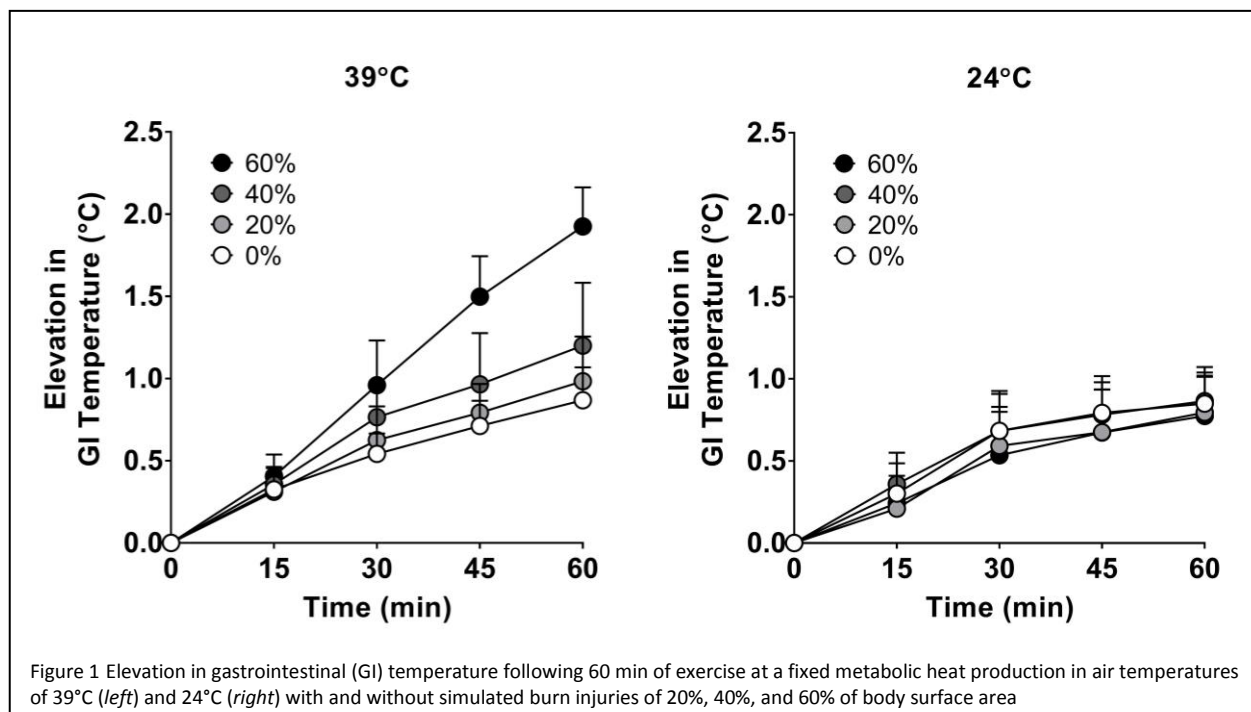
What was accomplished under these goals?: We are close to completing the project outlined in Aim 1A; we still need 1 large female and 2 small males to complete those protocols. We have identified and scheduled these three individuals, with an anticipated completion date of December 2017, assuming no cancelations. Data from Aim 1A has been presented at the annual American Burn Association meeting and the Military Health System Research

Symposium. We have initiated data collection for Aim 1B (assessment of the impact of large/small stature on thermoregulatory responses in actual burn victims). However, given the new approach (outlined in the 2016 annual report) where we will investigate multiple aims performed in burn survivors during one multi-day visit, we did not complete data collection for Aim 1B. This new approach is preferred to assessing individuals just for aim 1B, and then bringing them back for a unique visit at a later date to address the other aims specific to burned individuals. Regarding Aims 1B, 2D, and 4, which are also performed in survivors, that work has begun and we continue to actively recruit such individuals into these aims.

We are pleased to say that we are making very good progress in addressing Aims 2A and 2C. In fact, for Aim 2A we obtained sufficient data to present preliminary findings at the annual Experimental Biology meeting and we only need to complete a few more subjects to closeout that Aim. Below is the submitted abstract of that work as well as the primary findings (Figure 1). These data confirm that an individuals with 20% and 40% body surface area burn working at a moderate exercise intensity (6 W/kg) are able to regulate core body temperature at a similar level as that observed in non-burned while exposed to both thermoneutral and hyperthermic environmental conditions. However, individuals with a 60% body surface area burn are at a greater risk for a hyperthermic injury when performing moderate exercise in the heat, but not in thermoneutral conditions.

TITLE: Impact of air temperature on core temperature regulation during exercise using a simulated burn injury model

ABSTRACT: Following a burn injury, excision of injured skin and subsequent grafting lead to attenuated sweating rates and thereby a diminished capacity for evaporative heat loss, resulting in exacerbated elevations in core temperature and greater risk of heat illness during physical activities. Since the capacity for evaporation is dependent on the absolute area of non-injured body surface area (BSA), and the heat load imposed on the body reflects both metabolic and environmental sources of heat gain, the detrimental effect of a burn injury on core temperature regulation during exercise at a given intensity is likely dependent on the interaction between the size of a burn injury and the prevailing air temperature. To test this possibility, six healthy males (25 ± 5 years, 76.1 ± 11.5 kg, 1.92 ± 0.17 m²) visited the laboratory on eight occasions to complete 1 h of cycling at a fixed rate of metabolic heat production (~ 6 W/kg; indirect calorimetry) in a 39°C or 24°C environment (20% relative humidity) with a simulated burn injury of 0%, 20%, 40%, or 60% BSA (see figure below). Burn injuries were simulated by covering skin on the torso, arms, and legs with highly absorbent, vapor-impermeable material that impedes sweat evaporation. Core temperature was measured in the gastrointestinal tract (T_{gi}). Elevations in T_{gi} at 24°C were not different across all simulated burn injury levels (0%: $0.81 \pm 0.13^\circ\text{C}$, 20%: $0.70 \pm 0.20^\circ\text{C}$, 40%: $0.78 \pm 0.14^\circ\text{C}$, 60%: $0.65 \pm 0.16^\circ\text{C}$; $P \geq 0.32$). At 39°C, the increase in T_{gi} was not different between 0% ($0.83 \pm 0.24^\circ\text{C}$), 20% ($0.96 \pm 0.35^\circ\text{C}$), and 40% ($0.99 \pm 0.15^\circ\text{C}$) simulated burn injuries ($P \geq 0.60$), but the rise in T_{gi} with a 60% simulated burn injury ($1.84 \pm 0.16^\circ\text{C}$) was greater than the other “injury” levels ($P < 0.05$). Consistent with this observation, elevations in T_{gi} were exacerbated at 39°C *versus* 24°C only with a 60% simulated burn injury ($P < 0.01$). In summary, core temperature reached similarly elevated levels following 1 h of moderate-intensity exercise with simulated burn injuries of 20%, 40%, and 60% of BSA under temperate environmental conditions, and with simulated burn injuries of 20% and 40% in hot conditions. However, exercise in the heat at the same intensity with a 60% BSA simulated burn injury resulted in a greatly exacerbated elevation in T_{gi} . Therefore, burn survivors with injuries spanning 60% of total BSA may be exposed to a greater risk of hyperthermia and heat illness when working at a fixed intensity in a hot environment.



We are also making very good progress at accomplishing the objectives of Aim 2C, with five subjects either completing, or in various stages of completion, for this protocol.

What opportunities for training and professional development has the project provided?:

Though the project was not intended to provide training or professional development opportunities, training has nonetheless taken place as a result of the performed work. Specifically, Matt Cramer, Ph.D., Gilbert Morales, Ph.D., and Mu Huang, Ph.D. are postdoctoral fellows working on this project. As a result of this project, all three received training in the following areas: IRB approvals, subject recruitment (both uninjured and burned subjects), data collection and management, data analysis and reporting, and presentation of the data. Regarding the last point, data from these studies have been presented by trainees at weekly "Works in Progress" meetings, at the American Burn Association, at the World Burn Congress, at Experimental Biology 2017, and at the 2017 American College of Sports Medicine Meeting.

How were the results disseminated to communities of interest?: The obtained data have been presented at the following national and international meetings in verbal or poster formats: internal "Works in Progress" meetings, the American Burn Association, the World Burn Congress, the Military Health System Research Symposium, Experimental Biology, and the American College of Sports Medicine meeting. We expect that in the next year at least one, and possibly two publications will originate from the data obtained thus far.

What do you plan to do during the next reporting period to accomplish the goals?: Over the next 12 months we need to continue with enrollment and data collection for the studies that are already initiated (i.e., 1B, 2A, 2C, 2D, and 4). As mentioned above, these studies take a tremendous effort from both the research subject and the research team to complete, with some protocols requiring upwards to 9 unique laboratory visits to complete data collection from each subject for a specific protocol.

4. IMPACT

What was the impact on the development of the principal discipline of the project?:

The obtained data in Aim 1A indicate that the thermoregulatory consequence of a burn injury of a given relative size (e.g., 40% of total body surface area) is heavily influenced by the overall size of the individual. That is, a smaller individual having the exact same percentage of his/her body surface area burned is at a greater risk for a hyperthermic injury relative to a larger individual having the exact same percent body surface area burned. These data alone are sufficient to reconsider the Army's Standard of Medical Fitness requirement of a single qualifier stating that >40% body surface area burned "does not meet the standard", since if the burned individual is large s/he will be better able to tolerate a hyperthermic insult relative to if s/he were small.

Data from Aim 2A (though still preliminary but the findings are robust) will inform the military that individuals with a 20% and 40% body surface area burns are fully capable to regulating their internal temperature, when compared to a non-burned individual, exercising at moderate intensities in both normothermic and hyperthermic environments. However, individuals with 60% body surface area burn are at a greater risk for a hyperthermic injury, but only when exercising in conditions of elevated environmental temperatures.

What was the impact on other disciplines?: The obtained data will be of interest to the civilian burn rehabilitation community. Exercise is critical for appropriate rehabilitation. That said, burned individuals are often hesitant to perform aerobic exercise training for fear that they may experience a heat-related injury. The information presented above will be very beneficial to the rehabilitation community by instructing them that a larger person with the same percent body surface area will be better able to "thermally" tolerate exercise at a given rate of metabolic heat generation relative to a smaller person, thereby improving the safety of the rehabilitation of individuals with these injuries. The obtained data will also inform the rehabilitation community that individuals with burns up to (and including) 40% body surface area are fully capable of regulating body core temperature during moderate exercise in both normothermic and hyperthermic environmental conditions. However, individuals with 60% of their body surface area burned should be cautious when exercising at a moderate intensity in hyperthermic environmental conditions.

What was the impact on technology transfer?: Nothing to report.

What was the impact on society beyond science and technology?: Nothing to report.

5. CHANGES/PROBLEMS

Changes in approach and reason for change: None

Actual or anticipated problems or delays and actions or plans to resolve them: We have been frustrated in recruiting one large female and two small males necessary to complete Aim 1A. We previously had such individuals scheduled, but those subjects didn't complete the protocol (for varying reasons). We have identified and scheduled the remaining necessary subjects, resulting in an expected completion date of December, 2017, assuming no further cancelations. With that said, we would like to emphasize that the findings are so robust, even without the inclusion of these three subjects, that we are seeing very clear differences in the elevation in body core temperature between large and small individuals having a 40% body surface area simulated burn.

Recruitment of individuals having burn injuries is always challenging, let alone such individuals with fairly narrow inclusion criteria (e.g., large and small individuals having ~40% body surface area burned – Aim 1B). That said, we have recently tapped sources that has resulted in dozens of burned individuals expressing interest in participating in these research trials. These sources included email blasts via a burn support group's email list (Phoenix Society), facebook posting on that support group's page, direct mailings to prior burned individuals from the Parkland Hospital database, and recruitment of burned individuals attending the World Burn Congress. We are presently screening these individuals to determine eligibility for enrollment. Unfortunately, we have just about given up in working with the US Army to access their database of burned individuals. It is ironic that despite this project being funded by the US Army, we continue to not achieve any breakthroughs in accessing a database of burned individuals currently or previously in the Army. Our primary challenge in accessing the US Army's database of burned soldiers is identifying the appropriate individual(s) who can provide insight into how we could tap this valuable resource.

Changes that had a significant impact on expenditures: None

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents: No changes were enacted. The IRB protocols were approved and renewed on 5/17/2017, with an annual expiration date (requiring submission of continuing renewal) of 5/17/2018.

Significant changes in use or care of human subjects: None

Significant changes in use or care of vertebrate animals: None

Significant changes in use or care of biohazards and/or select agents: None

6. PRODUCTS

Publications, conference papers, and presentations:

Journal publications: None

Books or other non-periodical, one-time publications: Abstracts from this project were presented at the following meetings during the prior 12 months:

Experimental Biology
American College of Sports Medicine
American Burn Association
Military System Health Research Symposium

Other publications, conference papers, and presentations: Data from these projects were presented (in either oral or poster formats) at the meetings indicated above, as well as the World Burn Congress. Moreover, Matt Cramer, Ph.D. has presented data originating from this work internally at our "works in progress."

Website(s) or other Internet site(s): None

Technologies or techniques: None

Inventions, patent applications, and/or licenses: None

Other products: None

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name: Dr. Craig Crandall

Project Role: PI

Researcher Identifier:

Nearest person month worked: 4

Contribution to Project: Dr. Crandall has worked extensively with the lab team while planning and implementing data collection and analysis.

Funding Support: Dr. Crandall receives extramural funding from the Department of Defense and the NIH

Name: Matt Cramer, Ph.D.

Project Role: Post-doctoral fellow

Researcher Identifier:

Nearest person month worked: 9

Contribution to Project: Dr. Cramer assists with all aspects of the study, from recruitment through data analysis. This contribution has been quite extensive as each subject requires multiple visits to the laboratory to accomplish the stated aims.

Funding Support: Dr. Cramer receives extramural funding support from grants to Dr. Crandall from the NIH and the Department of Defense. He also receives salary support through the Natural Sciences and Engineering Research Council of Canada.

Name: Gilbert Moralez, Ph.D.

Project Role: Post-doctoral fellow

Researcher Identifier:

Nearest person month worked: 1

Contribution to Project: Dr. Moralez assists with data collection.

Funding Support: Dr. Moralez receives extramural funding support from grants to Dr. Crandall from the NIH.

Name: Mu Huang, Ph.D., DPT

Project Role: Post-doctoral fellow

Researcher Identifier:

Nearest person month worked: 1

Contribution to Project: Dr. Huang assists with data collection.

Funding Support: Dr. Huang receives salary support from the School of Health Professions at the University of Texas Southwestern Medical Center.

Name: Naomi Kennedy RN, BSN

Project Role: Research Nurse

Researcher Identifier:

Nearest person month worked: 3

Contribution to Project: Naomi has assisted with subject screening and consenting, data collection, and subject safety.

Funding Support: Ms Kennedy receives extramural funding support from grants to Dr. Crandall from the NIH and the Department of Defense

Name: Amy Adams, M.S.

Project Role: Research Associate

Researcher Identifier:

Nearest person month worked: 3

Contribution to Project: Ms Adams assists with subject recruitment, scheduling, and with data collection and reduction.

Funding Support: Ms Adams receives extramural funding support from grant to Dr. Crandall from the NIH and the Department of Defense

Name: Manall Jaffrey, M.S.

Project Role: Research Associate

Researcher Identifier:

Nearest person month worked: 1

Contribution to Project: Ms Jaffrey assists with subject recruitment, scheduling, and assisted with data collection and reduction.

Funding Support: Ms Jaffrey receives extramural funding support from grant to Dr. Crandall from the NIH and the Department of Defense

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?: Yes, a grant from the Department of Defense in which Dr. Crandall was the PI ended March 2017. The ending of this grant does not impact the support for the present project. No new other support has been received since the last reporting period.

What other organizations were involved as partners?: Nothing to report.

8. SPECIAL REPORTING REQUIREMENTS

Collaborative Awards: Not applicable

Quad Chart: See attachment

Effects of Burn Injuries on Thermoregulatory and Cardiovascular Responses in Soldiers: Implications for the Standards of Medical Fitness

BA150093

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PI: Craig Crandall, Ph.D.

Org: Univ of Texas Southwestern Medical Center Award Amount: \$2,017,168

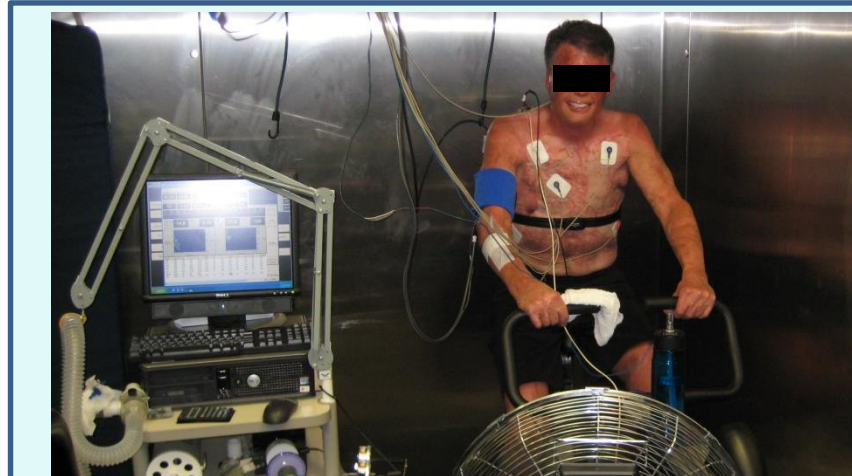


Study/Product Aim(s)

- Aim 1: Absolute body surface area (BSA) available for heat dissipation (i.e., uninjured skin) more accurately predicts thermoregulatory and cardiovascular consequences during a thermal stress relative to the current standard of using %BSA burned.
- Aim 2: The extent to which a burn injury is detrimental to an individual is dependent on the ambient temperature at a given exercise intensity and the exercise intensity within a given environment.
- Aim 3: Does the location of the burn injury influence thermoregulatory responses?
- Aim 4: Does the donor site contribute to compromised thermoregulatory responses in burned individuals.
- Aim 5: Identification of an upper limit for which a soldier with a prior burn injury could be expected to maintain a safe core body temperature across differing metabolic demands and environmental conditions.

Approach

The above questions will be addressed primarily by measuring thermoregulatory responses (e.g., core and skin temperatures) during exercise in neutral and hyperthermic environments at various workloads (e.g. rate of metabolic heat generation) in individuals with simulated burn injuries and in actual burn patients.



Accomplishment: We continue to collect data for Aim 1A and 1B and have initiated data collection for aims 2A, 2C, 2D and 4.

Timeline and Cost

Activities	CY	16	17	18	19	20
Aim 1: Body surface area						
Aim 2: Effect of workload and climate						
Aim 3: Burn location						
Aim 4: Donor site						
Aim 5: Compilation						
Estimated Budget (\$K)		\$431	\$375	\$395	\$399	\$419

Goals/Milestones

CY16 Goal – Obtain IRB and HRPO approvals. Initiate data collection for Aim 1A.

CY17 Goals – Complete Aims 1A and initiate Aims 2.

CY18 Goal – Continue data collection for Aims 1B, all Aim 2s, and Aim 4.

CY19 Goal – Complete data collection for Aim 2 and initiate data collection for Aim 3.

CY20 Goal – Complete data collection for Aims 1B, 3, and 4 (data collection for Aim 4 will occur throughout the funding period as suitable burned subjects are identified). Complete the synthesis of the obtained data and provide guidelines regarding burn injury size/location, environmental condition, and workload by which a burned soldier could safely perform his/her duties.

Comments/Challenges/Issues/Concerns

- We have done an exceptional job at recruiting subjects and accomplishing the grant's objectives. The only exception is identifying 2 small males to complete Aim 1B. With that said, we remain on track relative to our expected goals.

Budget Expenditure to Date

Projected Expenditure: \$805,668

Actual Expenditure: \$621,065.64

Updated: 10/16/2017