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TITLE: Permethrin Exposure Dosimetry: Biomarkers and Modifiable Factors

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| 14. ABSTRACT The primary aim of this project is to investigate the relationship between various modifiable factors and the absorption of permethrin as a result of wearing permethrin-treated Army Combat Uniforms (ACU-Permethrin). The research objective is to examine the effect of body weight/BMI and total energy expenditure on permethrin absorption and dose, as determined by measurement of urinary biomarkers (3PBA and cis- and trans-DCCA) levels. There are two studies involved in our project – the first is a study among Army recruits during Basic Training (Study 1) and the second involves Army National Guard Soldiers during Annual Training (Study 2). Data collection for Study 1 was completed in 2015. Data collection for Study 2 is in progress. | | | | | |
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Section 1: Introduction

The primary aim of this project is to investigate the relationship between various modifiable factors and the absorption of permethrin as a result of wearing permethrin-treated Army Combat Uniforms (ACU-Permethrin). The research objective is to examine the effect of body weight/BMI and total energy expenditure on permethrin absorption and dose, as determined by measurement of urinary biomarkers (3PBA and cis- and trans-DCCA) levels. There are two studies involved in our project – the first is a study among Army recruits during Basic Training (Study 1) and the second involves Army National Guard Soldiers during Annual Training (Study 2).

Section 2: Keywords

Permethrin, biomarkers, military, dose, exposure dosimetry, military, energy expenditure

Section 3: Accomplishments

3:1 - What were the major goals of the project?

As described in the approved Statement of Work (see Table of Tasks below), the major goals during the Year 2 of this project are outlined (see highlighted section).

| | | | |
|--------|----------------|---------------------|--|
| Year 1 | Task 1 | <i>Months 1-4</i> | -Project set up and approvals |
| | Task 2 | <i>Months 4-8</i> | -Plan logistics for Study 1 |
| | Task 3 | <i>Months 4-8</i> | -Study 1 protocol approval |
| | Task 4 | <i>Months 8-12</i> | -Initiate Study 1 data collection |
| | Task 5 | <i>Months 10-12</i> | -Initiate laboratory analyses of Study 1 samples |
| | Task 6 | <i>Months 10-12</i> | -Initiate Study 1 data management steps; integrate with USARIEM research database system |
| Year 2 | Task 7 | <i>Months 13-15</i> | -Prepare analytic dataset for data analyses |
| | Task 8 | <i>Months 15-17</i> | -Initiate Study 1 data analyses to address hypotheses |
| | Task 9 | <i>Months 14-20</i> | -Plan logistics for Study 2 |
| | Task 10 | <i>Months 14-20</i> | -Study 2 protocol approval |
| | Task 11 | <i>Months 16-24</i> | -Report/summarize Study 1 results |
| | Task 12 | <i>Months 20-24</i> | -Initiate Study 2 data collection |
| Year 3 | Task 13 | <i>Months 25-26</i> | -Initiate laboratory analyses of Study 2 samples |
| | Task 14 | <i>Months 25-30</i> | -Initiate Study 2 data management steps |
| | Task 15 | <i>Months 30-36</i> | -Complete Study 1 and Study 2 laboratory sample analyses |
| | Task 16 | <i>Months 37-39</i> | -Complete integration of analytic dataset for project data analyses |
| | Task 17 | <i>Months 37-39</i> | -Complete Study 2 data analyses to address hypotheses |

| | | | |
|---------------|----------------|---------------------|---|
| Year 4 | Task 18 | <i>Months 39-48</i> | -Report/summarize Study 2 results -Prepare Project technical reports/manuscripts for publication |
| | Task 19 | <i>Months 39-48</i> | -Provide/disseminate evidence-based guidance |

3:2 - What was accomplished under these goals?

TASKS 1-3 were completed in Year 1 (See last year's Annual Report.)

Below is a bulleted list of the projected goals and accomplishments over this Year 2 study period:

TASKS 4, 5, & 6 Initiate Study 1 data collection; Initiate laboratory analyses of Study 1 samples; & Initiate Study 1 data management steps [COMPLETE]

- The field study data collection for Study 1 with US Army recruits during their Basic Combat Training (BCT) period was initiated and completed at Ft. Sill OK (Oct-Dec 2015).
- Laboratory analyses of samples collected in Study 1 have been completed (as of July 2016).
- Data management steps, in terms of setting up the data collection instruments/surveys for Study 1 and making a plan for the integration of collected data into a study database has been completed.

Task 7 Prepare analytic dataset for data analyses [COMPLETE]

- Preparations for the Study 1 analytic dataset are underway.

Task 8 Initiate Study 1 data analyses to address hypotheses [COMPLETE]

- We received the Study 1 laboratory sample analyses results for total energy expenditure from Pennington Biomedical Research Center (PBRC) in January 2016.
- We received the Study 1 laboratory sample analyses results for the permethrin metabolite concentrations from the Centers for Disease Control (CDC) in mid-July 2016.
- We have integrated these data with the field study collected database and initiated data analyses to address the study hypotheses.

Task 9-Plan logistics for Study 2 [COMPLETE]

- The logistics and planning for Study 2 with the National Guard Bureau (NGB) for the participation of Army National Guard Soldiers during their Summer 2016 Annual Training period has been completed.
 - ◆ The NGB provided their endorsement of the study and communicated with state-level POCs on behalf of this study.
 - ◆ Approval from the TAG to conduct the study with Massachusetts ARNG Soldiers was obtained in May 2016.
 - ◆ Approval from the TAG to conduct the study with Maine ARNG Soldiers was obtained in July 2016.

Task 10 Study 2 protocol approval [COMPLETE]

- USARIEM IRB approval of Study 2 (#14-29HC) has been completed, with approval in May 2016 to conduct the study with the MA ARNG during their AT in early June (amendment #11, approved 26 May 2016). Approval in July 2016 to conduct the study with the ME ARNG during their AT in early August was recently approved (amendment #12, approved 22 July 2016).

Task 11 Report/summarize Study 1 results [IN PROGRESS]

- Analyses to address the Study 1 hypotheses are in progress.
- The study was of repeated measures design in which we saw the same group of Army recruit participants over the course of their ~9 week initial military training period. A total of 60 participants consented to participate.
- The mean age of the group was 21.3 (2.7) years of age and 30% female. The average weight on Day 1 of the study was 72.8 (13.1) kg [males: 76.8 (12.1); females 63.8 (10.6)]. The average % body fat measured on Day 1 was 14.8 (5.8) [males: 12.3 (4.8); females 20.3 (3.8)].
- Over the course of the study, a total of 8 participants withdrew (themselves) from the study (that is, they decided they no longer wanted to participate). And, also, over the course of the study, a total of 8 participants left the Army, were recycled, or otherwise didn't remain with the BCT group during the study period.

Task 12 Initiate Study 2 data collection [COMPLETE]

- Study 2 data collection with the MA ARNG was initiated and completed in June 2016, with a total of n=15 providing consent and n=14 persons participants completing the study.
- Data collection efforts for Study 2 are continuing with the ME ARNG in early August (4-12 Aug 2016).

We have also initiated several of the planned Year 3 tasks.

Task 13 Initiate laboratory analyses of Study 2 samples [IN PROGRESS]

- Laboratory analyses of the Study 2 samples collected in June are underway at CDC and PBRC. We have already received the results from PBRC for the total energy expenditure in early July 2016.

Task 14 Initiate Study 2 data management steps [COMPLETE]

- Data management steps, in terms of setting up the data collection instruments/surveys for Study 2 and making a plan for the integration of collected data into a study database has been completed.

3:3 - What opportunities for training or professional development has the project provided?

- A Boston University School of Public Health graduate student (MPH candidate) is currently working on this project; her primary role on the project is performing data management and analytic tasks for the project.
- A Boston University School of Public Health graduate student (PhD candidate) is currently working on this project; her primary role on the project is to help direct field data collection activities and in preparation of reports, abstract, manuscripts, and presentations.

3:4 - How were the results disseminated to communities of interest?

- Nothing to report at this point. We plan to send a EXSUM to the TRADOC Center for Initial Military Training when we complete the analyses of Study 1.

3:5 - What do you plan to do during the next reporting period to accomplish the goals?

- During the next reporting period, we expect the
 - completion of Study 2 field data collection
 - preparation and submission of papers and abstracts from Study 1

Section 4: Impact

4:1 - What was the impact on the development of the principle discipline of the project?

- Nothing to report at this point.

4:2 - What was the impact on other disciplines?

- Nothing to report at this point.

4:3 - What was the impact on technology transfer?

- Nothing to report at this point.

4:4 - What was the impact on society beyond science and technology?

- Nothing to report at this point

Section 5: Changes/Problems

5:1 - Changes in approach and reasons for change

- Nothing to report.

5:2 - Actual or anticipated problems or delays and actions or plans to resolve them

- As reported in last year's Annual Report, there was a lag in the start of Study 1 data collection in this study: it started at the beginning of Year 2 instead of the plan for the end of Year 1. But, now at the end of Year 2, we are back on track with our planned task schedule, as outlined in the approved SOW.

5:3 - Changes that had a significant impact on expenditures

- Nothing to report

5:4 - Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

- Nothing to report

Section 6: Products

6:1 - Publications, conference papers, and presentations

- Nothing to report

6:2 - Websites and/or Internet Sites

- Nothing to report

6:3 - Technologies or techniques

- Nothing to report

6:4 - Inventions, patent applications, and/or licenses

- Nothing to report

6:5 - Other products

- Nothing to report

Section 7: Participants and other Collaborating Organizations

7:1 - What individuals have worked on the project?

✓ *Name:* Susan P. Proctor, DSc

Project Role: Principal Investigator

Nearest person-month worked: 15% of 12 person-months (1.8 person-months)

Contribution to Project: Handling all PI responsibilities for the project, including interactions with the IRB, the grantee (HJF), CIMT, Army recruit training POCs, Fort Sill, NGB/ARNG, and CDC and PBRC staff.

Funding Support: Army Civilian employee

✓ *Name:* Matthew M. Scarpaci, MPH

Project Role: Project Coordinator

Nearest person-month worked: 100% of 12 person-months (12 person-months)

Contribution to Project: Mr. Scarpaci has assumed the role of project coordination, assisting the PI in the day-to-day planning of the project, IRB tracking, HJF administrative tasks, data collection preparations, and data management etc.

✓ *Name:* Alexis Maule, MPH

Project Role: Research Associate

Nearest person-month worked: 35% of 12 person-months (3 person-months)

Contribution to Project: Ms. Maule has continued to assist the PI and project coordinator on IRB-related tasks and training additional study staff on data collection processes.

Funding Support: Boston University employee supported through USARIEM IPA

✓ *Name:* Caitlin Dillon, BS

Project Role: Data Analyst

Nearest person-month worked: 50% of 12 months (6 person-months)- started June 2015 (ending late July 2016)

Contribution to Project: Ms. Dillon has worked on the set-up of data management tasks and work on database and analyses.

✓ *Name:* Nicole Murphy, BS

Project Role: Research Associate

Nearest person-month worked: 50% of 2 months (1 person-month)- started May 2016

Contribution to Project: Ms. Murphy has assisted in data collection processes.

7:2 - Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

- Nothing to report

7:3 - What other organizations were involved as partners?

- Nothing additional to report

Section 8: Special Reporting Requirements

8:1 – See Quad Report

Section 9: Appendices

Quad Report

Permethrin Exposure Dosimetry: Biomarkers and modifiable factors

Log Number: 13063057 Task Area: Biomarkers to monitor for injury and disease processes

Contract #: W81XWH-14-2-0130



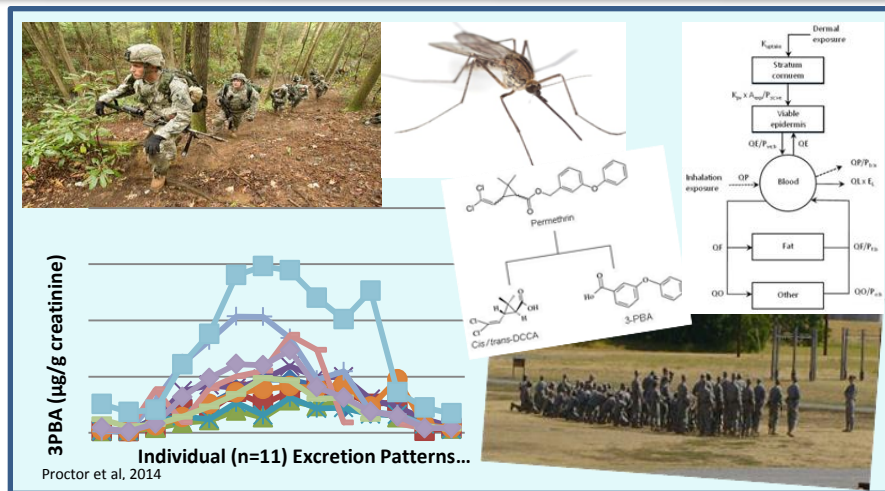
PI: Susan P. Proctor, DSc Org: Henry M. Jackson Foundation for the Advancement of Military Medicine (HJF) Award Amount: \$1,861,959

Study/Product Aim(s)

- Address the influence of permethrin exposure from wearing treated uniforms (ACU-Permethrin) on human dose and monitor the potential role of exposure on health and performance for accurate policy guidance regarding potential health risk.
- The study aims to determine the modifiable factors that significantly influence human permethrin dosimetry as a result of wearing the ACU-Permethrin. Specifically, determine whether body weight/body mass index and physical activity patterns influence the absorbed permethrin dose.

Approach

The project will define relationships between ACU-Permethrin wear-time scenarios among Army recruits (at Basic Training, Study 1) and Army National Guard Soldiers (during Annual Training, Study 2), urinary biomarkers of dose (3PBA, cis- and trans-DCCA), and modifiable factors (body mass index and physical activity levels) to provide valid predictive models.



Accomplishments [Yr2]: Study 1 data collection (with BCT recruits at Ft. Sill); sample analyses are complete and data analyses are in progress. Study 2 data collection is underway with the ARNG during their Annual Training period (in MA and ME locations).

Timeline and Cost

| Activities: | Yr 1 7/14- 6/15 | Yr 2 7/15- 6/16 | Yr 3 7/16- 6/17 | Yr 4 7/17- 6/18 |
|---|-----------------------|-----------------------|-----------------------|-----------------------|
| Project Start-Up/Approvals | █ | | | |
| Study 1 and Study 2 Data Collection and Sample Analysis | | █ | █ | |
| Data analyses & Preparation of Manuscript & Reports | | | █ | █ |
| Estimated Budget (\$K) | \$718 | \$521 | \$307 | \$316 |

Goals/Milestones

Yr1 Goals – Study approvals and Initiation of Study 1

- ✓ USARIEM IRB approval; HRPO approval granted Oct 2014
- ✓ Complete Study 1 site planning steps and initiate data collection

Yr2 Goals– Initiate Study 1 data analyses and Study 2 data collection

- ✓ Initiate Study 1 data analyses
- ✓ Complete Study 2 site planning steps and initiate data collection

Yr3 Goals– Complete Study 2 data collection and sample analyses

- Initiate Study 2 data analyses
- Complete Study 1 and 2 laboratory sample analyses

Yr4 Goals–Complete data analyses and manuscript(s) preparation

- Finalize data analyses and modeling
- Prepare technical reports/ manuscript(s)

Comments/Challenges/Issues/Concerns

- None, all on track

Budget Expenditure to Date:

Projected Expenditure: ~\$1100K

Actual Expenditure (as of 21 July 2016): 865K