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AWARD NUMBER: W81XWH-12-2-0023

TITLE: Prehospital Air Medical Plasma (PAMPer) Trial

PRINCIPAL INVESTIGATOR: Jason L. Sperry, MD, MPH

CONTRACTING ORGANIZATION: University of Pittsburgh

REPORT DATE: Sept 2020

TYPE OF REPORT: Final

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Fort Detrick, Maryland 21702-5012

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6. AUTHOR(S)

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

To determine the effect of the prehospital infusion (i.e., during air medical transport) of AB plasma or low titer anti-B A plasma (2 units) on 30-day mortality in patients with hemorrhagic shock as compared to standard air medical care.

Determine whether prehospital infusion of AB plasma or low titer anti-B A plasma (2 units) as compared to standard air medical care results in a reduction in 30-day mortality.

Determine whether prehospital infusion of AB plasma or low titer anti-B A plasma as compared to standard air medical care results in a lower 24-hour blood transfusion requirement, a lower incidence of multiple organ failure, nosocomial infection, acute lung injury and TRALI.

15. SUBJECT TERMS
Traumatic hemorrhagic shock, thawed plasma, prehospital

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		19b. TELEPHONE NUMBER *(include area code)*

1. **INTRODUCTION:**
   To determine the effect of the prehospital infusion (i.e., during air medical transport) of AB plasma or low titer anti-B A plasma (2 units) on 30-day mortality in patients with hemorrhagic shock as compared to standard air medical care.
   Determine whether prehospital infusion of AB plasma or low titer anti-B A plasma (2 units) as compared to standard air medical care results in a reduction in 30-day mortality.
   Determine whether prehospital infusion of AB plasma or low titer anti-B A plasma as compared to standard air medical care results in a lower 24-hour blood transfusion requirement, a lower incidence of multiple organ failure, nosocomial infection, acute lung injury and TRALI.

2. **KEYWORDS:** Provide a brief list of keywords (limit to 20 words).
   Traumatic hemorrhagic shock, thawed plasma, prehospital

3. **OVERALL PROJECT SUMMARY:** Summarize the progress during appropriate reporting period (single annual or comprehensive final). This section of the report shall be in direct alignment with respect to each task outlined in the approved SOW in a summary of Current Objectives, and a summary of Results, Progress and Accomplishments with Discussion. Key methodology used during the reporting period, including a description of any changes to originally proposed methods, shall be summarized. Data supporting research conclusions, in the form of figures and/or tables, shall be embedded in the text, appended, or referenced to appended manuscripts. Actual or anticipated problems or delays and actions or plans to resolve them shall be included. Additionally, any changes in approach and reasons for these changes shall be reported. **Any change that is substantially different from the original approved SOW (e.g., new or modified tasks, objectives, experiments, etc.) requires review by the Grants Officer's Representative and final approval by USAMRAA Grants Officer through an award modification prior to initiating any changes.**
   - Secondary analysis of samples has begun and is ongoing!

4. **KEY RESEARCH ACCOMPLISHMENTS:** Bulleted list of key research accomplishments emanating from this research. Project milestones, such as simply completing proposed experiments, are not acceptable as key research accomplishments. Key research accomplishments are those that have contributed to the major goals and objectives and that have potential impact on the research field.

University of Pittsburgh Coordinating Center	- Received IRB Annual Renewal approval on 11-AUG-2019. - Received HRPO Continuing Review approval on 24-SEP-2019.
ENROLLING SITES	
University of Pittsburgh Performance Site	- Received IRB Annual Renewal approval on 12-SEP-2019. - Received HRPO Continuing Review approval on 13-NOV-2019.
University of Louisville	- Received HRPO Continuing Review approval on 14-AUG-2019. - Received IRB Annual Renewal approval on 02-JUN-2020. - Submitted HRPO Continuing Review on 05-JUN-2020; pending acknowledgement.
MetroHealth	- Received IRB Annual Renewal approval on 01-JAN-2020. - Received HRPO Continuing Review approval on 22-APR-2020.
UT Southwestern (UTSW)	- Received HRPO Continuing Review approval on 14-AUG-2019. - Site plans to close-out their IRB; *pending documents*.
Harris (UTSW Subsite)	*IRB closed – no further action*
JPS (UTSW Subsite)	- Received HRPO Continuing Review approval on 14-AUG-2019. - Received IRB Closure/Final Report documents on 16-JAN-2020

	- Submitted HRPO Closure request on 08-APR-2020; *pending acknowledgement.*
University of Tennessee	- Received IRB Annual Renewal approval on 23-SEP-2019. - Received HRPO Continuing Review approval on 13-NOV-2019.
Vanderbilt University	- Received IRB Annual Renewal approval on 11-JUL-2019. - Received HRPO Continuing Review approval on 24-SEP-2019. - Received IRB approval for change in PI on 17-FEB-2020. - Received HRPO approval for change in PI on 11-MAR-2020. - Submitted HRPO Closure request on 25-JUN-2020; *pending acknowledgement.*

ENROLLMENT AS OF 15-SEP-2017 (date enrollment goal was reached):

Site	Total Enrollment	W/D	Excluded	TOTAL ITT ANALYSIS
Pittsburgh	150	0	14	136
Altoona	19	1	0	18
Vanderbilt	97	1	8	88
UTSW	42	1	2	39
Harris	21	1	0	20
JPS	2	0	0	2
MetroHealth	52	6	4	42
Tennessee	117	2	11	104
Louisville	64	8	4	52
Total	564	20	43	**501**

5. CONCLUSION: Summarize the importance and/or implications with respect to medical and /or military significance of the completed research including distinctive contributions, innovations, or changes in practice or behavior that has come about as a result of the project. A brief description of future plans to accomplish the goals and objectives shall also be included.

- The study concluded that for patients at risk for hemorrhagic shock, the administration of thawed plasma during prehospital air medical transport was safe and resulted in lower 30-day mortality and a lower median prothrombin-time ratio than standard-care resuscitation.
- A meeting with Investigators to discuss secondary analyses and manuscripts is anticipated to be held in the upcoming quarter.

6. PUBLICATIONS, ABSTRACTS, AND PRESENTATIONS:

a. List all manuscripts submitted for publication during the period covered by this report resulting from this project. Include those in the categories of lay press, peer-reviewed scientific journals, invited articles, and abstracts. Each entry shall include the author(s), article title, journal name, book title, editors(s), publisher, volume number, page number(s), date, DOI, PMID, and/or ISBN.

(1) Lay Press: ***Nothing to report***

(2) Peer-Reviewed Scientific Journals:

- **CHARACTERIZATION OF UNEXPECTED SURVIVORS FOLLOWING A PREHOSPITAL PLASMA RANDOMIZED TRIAL.** Gruen DS, Guyette FX, Brown JB, Daley BJ, Miller RS, Harbrecht BG, Claridge JA, Phelan HA, Yazer MH, Neal MD, Zuckerbraun BS, Sperry JL.Gruen DS, et al. Among authors: Sperry JL. J Trauma

Acute Care Surg. 2020 May 27. doi: 10.1097/TA.0000000000002816. Online ahead of print.J Trauma Acute Care Surg. 2020. PMID: 32472902

- **Forgot calcium? Admission ionized-calcium in two civilian randomized controlled trials of prehospital plasma for traumatic hemorrhagic shock.** Moore HB, Tessmer MT, Moore EE, Sperry JL, Cohen MJ, Chapman MP, Pusateri AE, Guyette FX, Brown JB, Neal MD, Zuckerbraun B, Sauaia A.Moore HB, et al. Among authors: Sperry JL. J Trauma Acute Care Surg. 2020 May;88(5):588-596. doi: 10.1097/TA.0000000000002614.J Trauma Acute Care Surg. 2020. PMID: 32317575
- **Prehospital plasma is associated with distinct biomarker expression following injury.** Gruen DS, Brown JB, Guyette FX, Vodovotz Y, Johansson PI, Stensballe J, Barclay DA, Yin J, Daley BJ, Miller RS, Harbrecht BG, Claridge JA, Phelan HA, Neal MD, Zuckerbraun BS, Billiar TR, Sperry JL; PAMPer study group.Gruen DS, et al. Among authors: Sperry JL. JCI Insight. 2020 Apr 23;5(8):e135350. doi: 10.1172/jci.insight.135350.JCI Insight. 2020. PMID: 32229722
- **Massive transfusion and the response to prehospital plasma: It is all in how you define it.** Sim ES, Guyette FX, Brown JB, Daley BJ, Miller RS, Harbrecht BG, Claridge JA, Phelan HA, Neal MD, Forsythe R, Zuckerbraun BS, Sperry JL; PAMPer study group.Sim ES, et al. Among authors: Sperry JL. J Trauma Acute Care Surg. 2020 Jul;89(1):43-50. doi: 10.1097/TA.0000000000002639.J Trauma Acute Care Surg. 2020. PMID: 32118820
- **Accelerating availability of clinically-relevant parameter estimates from thromboelastogram point-of-care device.** Pressly MA, Parker RS, Neal MD, Sperry JL, Clermont G.Pressly MA, et al. Among authors: Sperry JL. J Trauma Acute Care Surg. 2020 May;88(5):654-660. doi: 10.1097/TA.0000000000002608.J Trauma Acute Care Surg. 2020. PMID: 32032282
- **Association of Prehospital Plasma Transfusion With Survival in Trauma Patients With Hemorrhagic Shock When Transport Times Are Longer Than 20 Minutes: A Post Hoc Analysis of the PAMPer and COMBAT Clinical Trials.** Pusateri AE, Moore EE, Moore HB, Le TD, Guyette FX, Chapman MP, Sauaia A, Ghasabyan A, Chandler J, McVaney K, Brown JB, Daley BJ, Miller RS, Harbrecht BG, Claridge JA, Phelan HA, Witham WR, Putnam AT, Sperry JL.Pusateri AE, et al. Among authors: Sperry JL. JAMA Surg. 2019 Dec 18;155(2):e195085. doi: 10.1001/jamasurg.2019.5085. Online ahead of print.JAMA Surg. 2019. PMID: 31851290
- **Severity of hemorrhage and the survival benefit associated with plasma: Results from a randomized prehospital plasma trial.** Anto VP, Guyette FX, Brown J, Daley B, Miller R, Harbrecht B, Claridge J, Phelan H, Neal M, Forsythe R, Zuckerbraun B, Sperry J; PAMPer study group.Anto VP, et al. Among authors: Sperry J. J Trauma Acute Care Surg. 2020 Jan;88(1):141-147. doi: 10.1097/TA.0000000000002530.J Trauma Acute Care Surg. 2020. PMID: 31688793
- **Prehospital plasma in injured patients is associated with survival principally in blunt injury: Results from two randomized prehospital plasma trials.** Reitz KM, Moore HB, Guyette FX, Sauaia A, Pusateri AE, Moore EE, Hassoune A, Chapman MP, Daley BJ, Miller RS, Harbrecht BG, Claridge JA, Phelan HA, Brown JB, Zuckerbraun BS, Neal MD, Yazer MH, Sperry JL.Reitz KM, et al. Among authors: Sperry JL. J Trauma Acute Care Surg. 2020 Jan;88(1):33-41. doi:

10.1097/TA.0000000000002485.J Trauma Acute Care Surg. 2020. PMID: 31524836

- **Implementation of a prehospital air medical thawed plasma program: Is it even feasible?** Adams PW, Warren KA, Guyette FX, Yazer MH, Brown JB, Daily BJ, Miller RS, Harbrecht BG, Claridge JA, Phelan HA, Witham WR, Putnam AT, Zuckerbraun BS, Neal MD, Sperry JL; PAMPer study group.Adams PW, et al. Among authors: Sperry JL. J Trauma Acute Care Surg. 2019 Nov;87(5):1077-1081. doi: 10.1097/TA.0000000000002406.J Trauma Acute Care Surg. 2019. PMID: 31205211
- **Prehospital Blood Product and Crystalloid Resuscitation in the Severely Injured Patient: A Secondary Analysis of the Prehospital Air Medical Plasma Trial.** Guyette FX, Sperry JL, Peitzman AB, Billiar TR, Daley BJ, Miller RS, Harbrecht BG, Claridge JA, Putnam T, Duane TM, Phelan HA, Brown JB.Guyette FX, et al. Among authors: Sperry JL. Ann Surg. 2019 Apr 13. doi: 10.1097/SLA.0000000000003324. Online ahead of print.Ann Surg. 2019. PMID: 30998533

(3) Invited Articles: ***Nothing to report***

(4) Abstracts: ***Nothing to report***

b. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.

- WTA 2019: Implementation of a prehospital air medical thawed plasma program: Is it even feasible?
- AAST 2019:
  - Severity of hemorrhage and the survival benefit associated with plasma: Results from a randomized prehospital plasma trial.
  - Prehospital plasma in injured patients is associated with survival principally in blunt injury: Results from two randomized prehospital plasma trials.
- American College of surgeons 2019: Prehospital plasma and who benefits most
- EAST 2020: Massive transfusion and the response to prehospital plasma: It is all in how you define it.
- WTA 2020: CHARACTERIZATION OF UNEXPECTED SURVIVORS FOLLOWING A PREHOSPITAL PLASMA RANDOMIZED TRIAL.
- NorthWestern Trauma Symposium: Prehospital Plasma: Where the Signal Is
- 2019 Southwest Trauma & Acute Care Symposium: Prehospital Plasma
- CTTACC meeting 2019: Pamper and whole blood
- Detroit Trauma Symposium 2019: Prehospital Plasma: What's the Evidence

7. INVENTIONS, PATENTS AND LICENSES: List all inventions made and patents and licenses applied for and/or issued. Each entry shall include the inventor(s), invention title, patent application number, filing date, patent number if issued, patent issued date, national, or international. ***Nothing to report***

8. REPORTABLE OUTCOMES: Provide a list of reportable outcomes that have resulted from this research. Reportable 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. This list may include development of prototypes, computer programs and/or software (such as databases and animal models, etc.) or similar products that may be commercialized.

- The study concluded that for patients at risk for hemorrhagic shock, the administration of thawed plasma during prehospital air medical transport was safe and resulted in lower 30-day mortality and a lower median prothrombin-time ratio than standard-care resuscitation.

9. **OTHER ACHIEVEMENTS:** This list may include degrees obtained that are supported by this award, development of cell lines, tissue or serum repositories, funding applied for based on work supported by this award, and employment or research opportunities applied for and/or received based on experience/training supported by this award.
   Nothing to report

   For each section, 4 through 9, if there is no reportable outcome, state "Nothing to report."

10. **REFERENCES:** List all references pertinent to the report using a standard journal format (i.e., format used in *Science*, *Military Medicine*, etc.).

11. **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.
    Nothing to report

NOTE:

TRAINING OR FELLOWSHIP AWARDS: For training or fellowship awards, in addition to the elements outlined above, include a brief description of opportunities for training and professional development. Training activities may include, for example, courses or one-on-one work with a mentor. Professional development activities may include workshops, conferences, seminars, and study groups.

Nothing to report

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.

Nothing to report

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

MARKING OF PROPRIETARY INFORMATION: Data that was developed partially or exclusively at private expense shall be marked as "Proprietary Data" and Distribution Statement B included on the cover page of the report. Federal government approval is required before including Distribution Statement B. The recipient/PI shall coordinate with the GOR to obtain approval. REPORTS NOT PROPERLY MARKED FOR LIMITATION WILL BE DISTRIBUTED AS APPROVED FOR PUBLIC RELEASE. It is the responsibility of the Principal Investigator to advise the GOR when restricted limitation assigned to a document can be downgraded to "Approved for Public Release." DO NOT USE THE WORD "CONFIDENTIAL" WHEN MARKING DOCUMENTS. See term entitled "Intangible Property – Data and Software Requirements" and https://mrmc.amedd.army.mil/index.cfm?pageid=researcher_resources.technical_reporting for additional information.