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TITLE: "Serum and Exudate Calcitonin Precursors as Predictors of Wound Infection
and Dehiscence in Wartime Penetrating Injuries"

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14. ABSTRACT Patient enrollment has rapidly accelerated in the past few months, in part due to re-doubling of recruitment efforts and in part due to increased casualty flow. To date 124 patients have been enrolled into the study that have either been wounded in Iraq or Afghanistan and 5 control tissue patients who have had their patella tendon repaired and donated pieces of the Autologous tendon. Due the increased patient enrollment the period of performance has been extended to further ensure adequate data and study power to definitively answer the clinical questions we are investigating regarding the relationship of serum and wound cytokines and chemokines and wound healing in our combat-wounded warriors.					
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INTRODUCTION:

This controlled variable study will demonstrate that ProCT and other cytokines are detectable in wound exudate. It will also determine the sensitivity, specificity, and both positive and negative predictive values of serum and exudate ProCT/cytokines with respect to wound dehiscence and infection. Finally, it will compare the efficacy of serum or exudate ProCT/cytokine levels to established serum or exudate markers for infection in predicting the risk of wound infection and dehiscence. Participants of this study are wounded U.S. service members that sustain high-energy penetrating injuries to a single extremity and evacuated from Iraq, Afghanistan and any future area of US combat operations that are admitted to Walter Reed Army Medical Center (WRAMC) or National Naval Medical Center (NNMC). Local antibiotic delivery, high-pressure irrigation and wound evacuation dressings have advanced the treatment of high-energy penetrating injuries, but the decision to primarily close or perform flap coverage of a wound remains subjective. Considerable intra-observer variability exists and despite meticulous debridements and antibiotic therapy, some clean appearing wounds go on to dehiscence and become infected. Conversely, because of this uncertainty, benign appearing wounds may undergo unnecessary surgical debridements, exposing patients to additional anesthesia risks and surgical morbidity. A serum or exudate marker that correlates with wound dehiscence and infection could prevent life and limb-threatening complications caused by premature wound closure and eliminate the morbidity associated with unnecessary debridement procedures.

BODY:

Project accomplishments include: continued development of infrastructure to implement AIM I, AIMS II, & III; hiring and training of a second Research Assistant to assist with study supervision, sample handling, and data entry; and coordination with key personnel conducted including correspondence with study consultants, study statistician, and critical contacts at processing facilities, NMRC and VAMC. In addition, techniques for collection, processing and shipment of serum and exudate samples have been established and executed. Systems have been implemented to identify, screen, and enroll incoming patients that meet inclusionary criteria. The following is the enrollment for the past year (1 July 2009 to 30 June 2010) 68 patients have been enrolled into the study; 36 patient enrolled from National Naval Medical Center and 32 from Walter Reed Army Medical Center for a total of 68 patients enrolled into this study. The total enrollment since this study has been initiated is 124 patients enrolled.

KEY RESEARCH ACCOMPLISHMENTS:

Administrative and logistical matters.

a. Personnel.

- 1) Dr. Benjamin Kyle Potter has been identified as the interim study PI while Dr. Forsberg is completing his two year fellowship.

- 2) Mr. Wesley Stepp, Research Assistant, was transferred to another assignment but continued to support this study at a 5 % effort.
- 3) Ms. Xochitl Cenicerros, Research Assistant, resigned her position with this study 1 January 2010.
- 4) Mr Samuel Han was hired to replace Ms Cenicerros 22 December 2009. Mr Han, Research Assistant, is currently supporting the study at 100% effort and is primarily consenting and sampling patients at both NNMC and WRAMC. Mr. Han has also taken over cleaning up the database and along with minor alterations to enhance data manipulation.
- 5) Fred Gage PhD has supervised Research Assistants while continuing to provide study support through patient sampling and data collection.

b. Database.

- 1) Data collected and data entered into study database.
- 2) Minor alteration of study database completed to enhance data manipulation ability during data analysis phase.

c. Equipment. No Capital Equipment was purchased this past year.

d. Materials, supplies and consumables. Supplies and materials for NNMC, NMRC, VAMC, and WRAMC study requirements continue to be coordinated.

e. Institutional Review Board.

- 1) National Naval Medical Center (NNMC). There has been four (4) protocol amendments made by Responsible Conduct of Research Department at NNMC.
 - A) Change in Principal Investigator from Dr. Jonathan Forsberg to Dr. Benjamin Potter as Dr. Forsberg went to New York for his Fellowship Training; Dr Forsberg was changed to an Associate Investigator.
 - B) Ms Cenicerros resigned her position and was removed as an Associate Investigator; Mr Samuel Han became an Associate Investigator to replace Ms Cenicerros.
 - C) Control tissue collection was added to the protocol.
 - D) Change in the Negative Pressure machine went from an older model to a newer model.
- 2) Walter Reed Army Medical Center (WRAMC) There has been four (4) protocol amendments by DCI at WRAMC this past year.
 - A) Dr. Potter became Principal Investigator as Dr. Forsberg went to New York for his Fellowship Training. Dr. Forsberg was changed to an Associate Investigator.
 - B) Ms Cenicerros was removed as Associate Investigator due to her resignation; Mr Samuel Han was added as an Associate Investigator.
 - C) Dr. Fred O'Brien was added as an Associate Investigator.
 - D) Control tissue collection was added as an amendment.

- 3) Completion of NNMC IRB Continuing Review 18 March 2010 and renewed approval of NNMC protocol Informed Consent Forms (ICF) and Health Insurance Portability and Accountability Act (HIPAA) forms 02 APRIL 10.
- 4) Completion of WRAMC IRB Continuing Review and renewed approval of WRAMC protocol Informed Consent Forms (ICF) and Health Insurance Portability and Accountability Act (HIPAA) forms.

f. Subject Enrollment.

- 1) Collection of data for AIM II & III has been conducted.
- 2) Currently 68 subjects have been enrolled and consented into the study Protocol; 36 patient enrolled from National Naval Medical Center and 32 from Walter Reed army Medical Center for a total of 68 patients enrolled into this study. The total enrollment since this study has been initiated is 124 patients enrolled.
- 3) Data collected has been continued to be entered into the study database.
- 4) Samples have been forwarded to VA and NMRC for analysis.

g. General

- 1) A no-cost extension was approved by the sponsor to extend research through 31 January 2011 with the final report due 28 February 2011.

REPORTABLE OUTCOMES: None

CONCLUSION: We have consented and collected data from 124 patients total since the study began, 68 the past year have been enrolled into the study at NNMC and WRAMC. We have started collecting control tissue from the autologous patella tissue transplants in the past year. We have not analyzed the data but continue to collect data and enroll patients. The period of performance has been extended to maximize the volume of patients enrolled and amount of data generated by the study.

REFERENCES: None

APPENDICES: None

SUPPORTING DATA: None