

AD-A166 550

NTC FILE COPY

Best Available Copy

AD _____

①

REPORT NUMBER #1

EIGHTH ANNUAL SHOCK SOCIETY MEETING

FINAL REPORT

Sherwood M. Reichard
James A. Cook
Daniel L. Traber
Robert F. Bond

November 1, 1985

Supported by

U. S. ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND
Fort Detrick, Frederick, Maryland 21701

Contract No. DAMD 17-85-G-5027

Shock Society
Medical College of Georgia
Augusta, GA 30912

DTIC
ELECTE
APR 11 1986
S E D

Approved for public release; distribution unlimited.

The findings in this report are not to be construed as an official Department of Army position unless so designated by other authorized documents.

20030121131

86 4 10 067

REPORT DOCUMENTATION PAGE

1a. REPORT SECURITY CLASSIFICATION UNCLASSIFIED			1b. RESTRICTIVE MARKINGS		
2a. SECURITY CLASSIFICATION AUTHORITY			3. DISTRIBUTION/AVAILABILITY OF REPORT Approved for public release; distribution unlimited.		
2b. DECLASSIFICATION/DOWNGRADING SCHEDULE			5. MONITORING ORGANIZATION REPORT NUMBER(S)		
4. PERFORMING ORGANIZATION REPORT NUMBER(S)			7a. NAME OF MONITORING ORGANIZATION		
6a. NAME OF PERFORMING ORGANIZATION Shock Society		6b. OFFICE SYMBOL (If applicable)	7b. ADDRESS (City, State, and ZIP Code)		
6c. ADDRESS (City, State, and ZIP Code) Medical College of Georgia Augusta, Georgia 30912			9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER DAMD17-85-G-5027		
8a. NAME OF FUNDING/SPONSORING ORGANIZATION U.S. Army Medical Research & Development Command		8b. OFFICE SYMBOL (If applicable)	10. SOURCE OF FUNDING NUMBERS		
8c. ADDRESS (City, State, and ZIP Code) Fort Detrick Frederick, Maryland 21701-5012		PROGRAM ELEMENT NO. 62772A	PROJECT NO. 3S1-62772A874	TASK NO. AB	WORK UNIT ACCESSION NO. 284
11. TITLE (Include Security Classification) Eighth Annual Shock Society Meeting					
12. PERSONAL AUTHOR(S) Reichard, Sherwood; Cook, James A.; Traber, Daniel L.; and Bond, Robert F.					
13a. TYPE OF REPORT Final	13b. TIME COVERED FROM 85/5/1 TO 85/11/1		14. DATE OF REPORT (Year, Month, Day) 1985 Nov 1		15. PAGE COUNT 8
16. SUPPLEMENTARY NOTATION					
17. *CONT'D COSATI CODES			18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)		
FIELD	GROUP	SUB-GROUP	Shock, Circulatory Shock, Sepsis, Shock Treatment, Eicosanoids, Lung, ARDS, Vasculature		
06	05				
06	16				
19. ABSTRACT (Continue on reverse if necessary and identify by block number) See attached summaries of Symposia I on Eicosanoids in and out of Shock, chaired by James A. Cook, Ph.D., Medical University of South Carolina and J. Raymond Fletcher, MD, PhD, Vanderbilt University, Symposia II, the Lung in Shock chaired by Daniel L. Traber, Ph.D. University of Texas, and Ulf Haglund, M.D., Ph.D., University of Lund, Sweden and Symposia III, Vascular Smooth Muscle Control chaired by Robert F. Bond, Ph.D., Oral Roberts University and Bart Churnow, M.D., Bethesda Hospital. For details of program and abstracts of presented papers see <u>CIRCULATORY SHOCK</u> , 1985. VOL. 16: 29-101, published by Alan R. Liss, Inc., 41 E. 11th St., New York, NY 10003.					
20. DISTRIBUTION/AVAILABILITY OF ABSTRACT ☐ UNCLASSIFIED/UNLIMITED ☒ SAME AS RPT. ☐ DTIC USERS			21. ABSTRACT SECURITY CLASSIFICATION UNCLASSIFIED		
22a. NAME OF RESPONSIBLE INDIVIDUAL Jane Idoine			22b. TELEPHONE (Include Area Code) 301/663-7325		22c. OFFICE SYMBOL SGRD-RMS

INTRODUCTION

The Eighth Annual Meeting of the Shock Society was held June 9-June 12, 1985 at Baltimore, Maryland. This report summarizes three symposia held at the meeting. Details of the program and abstracts of presented papers are available in CIRCULATORY SHOCK, 1985, VOL. 16: 29-101, published by Alan R. Liss, Inc., 41 E. 11th St., New York, NY 10003.

Accession For	
NTIS GRA&I	☒
DTIC TAB	☐
Unannounced	☐
Justification	
By	
Distribution/	
Availability Codes	
Dist	Avail and/or Special
A-1	



SYMPOSIUM I

EICOSANOIDS IN AND OUT OF SHOCK

James A. Cook, Ph.D., Medical University of South Carolina

J. Raymond Fletcher, M.D., Ph.D., Vanderbilt University

Dr. Bryan Smith gave an overview of the biological importance of eicosanoids concerning a brief summary of what is currently known about lipoyxygenase and cyclo-oxygenase enzymatic pathways and their structure and function. Dr. Perry Halushka gave a talk on the role of eicosanoids in disease states other than shock. In particular, he focused his presentation on diabetes mellitus, a disease state characterized by increased platelet aggregability and increased platelet thromboxane A_2 synthesis. My presentation dealt with the importance of cyclo-oxygenase products in shock-like states. The temporal sequence of thromboxane A_2 and prostaglandin synthesis in endotoxic shock was discussed and their effect on certain hemodynamic and hematologic sequelae. Potential interactions of cyclo-oxygenase and lipoyxygenase products in endotoxemia was also discussed. Dr. Dietrich Keppler discussed the role of leukotrienes in endotoxin action. He provided evidence for increased synthesis of leukotrienes in endotoxic shock and the beneficial effects of lipoyxygenase inhibitors and leukotriene receptor antagonists. The symposium was ended with a presentation by Dr. Raymond Fletcher concerning the significance of eicosanoids in medicine and clinical implications for shock therapy. Evidence for increased synthesis of cyclo-oxygenase products in patients with sepsis was presented. He also discussed what is known experimentally about the beneficial effects of certain cyclo-oxygenase inhibitors and their potential use as adjunctive therapy in patients with sepsis.

→ Contents Note: Biological Importance of Eicosanoids; The Role of Eicosanoids in Disease States Other Than Shock; The Importance of Cyclo-Oxygenase Products in Shock-like states; The Role of Leukotrienes in Endotoxin Action; The Significance of Eicosanoids in Medicine and Clinical Implications for Shock Therapy; Adult Respiratory Distress Syndrome; Lung Condition following Burn Injury; Lung Condition following Trauma and Hypovolemia; The Lung in Sepsis.

Shock Society Symposia

SYMPOSIUM II

Summary of Symposium for the Shock Society

The Lung in Shock - Dr. Daniel Traber and Dr. Haglund, Chairmen

The first speaker, Dr. Roger Spragg, presented a talk on adult respiratory distress syndrome -- general overview. Dr. Spragg discussed the fact that adult respiratory distress syndrome was a major cause of morbidity and mortality in trauma and septic patients. This entity had a 60% mortality associated with it. The individuals that survived the injury associated with this disease of the microvasculature oftentimes became permanently debilitated from a pulmonary standpoint. The disease itself is first manifested as a pulmonary edema. The edema itself is associated with depositions of polymorphonuclear cells in the pulmonary microvasculature with damage to the endothelial (alveolar type I) cells. Lavage materials obtained from patients also show that antiproteases have been inhibited either by complexing with proteolytic enzymes or interacting with oxygen free radicals. These same studies show a deficiency of surfactant materials in the area. As the patients recover from injury, there is a marked increase in the numbers of alveolar type 2 cells lining the alveolar capillary areas.

The next speaker on the program was Dr. George Kramer, who discussed the lung following burn injury. The data he presented indicated that there was not marked lung damage in this injury to the skin. There is an edema formation, but unlike the adult respiratory distress syndrome, this edema was associated with a low protein content. The vasoconstrictor thromboxane is also present in the pulmonary lymph, indicative of the formation of edema fluid, as a result of an increase in the microvascular pressure. Some investigators have reported a permeability type of pulmonary edema in burned rats; this has not been substantiated in other animal species, however. In individuals who have sustained injuries to the lung as a result of the inhalation of smoke there is a pulmonary edema again associated with the deposition of polymorphonuclear cells, apparently the result of an interaction of the chemicals of smoke with cells in the lung which release chemotactic factors.

The next speaker was Dr. Gunther Schlag, who spoke on the lung following trauma and hypovolemia. Here it was demonstrated that lung microvascular damage, increase in microvascular permeability, and shock followed multiple trauma and hypovolemia. Again, this damage to the microvasculature occurred as a result of an activation of polymorphonuclear cells, their deposition and degranulization in the pulmonary vasculature, their release of proteolytic enzymes and a fall in active antiprotease activities.

The next talk was presented by Dr. Traber and entitled "The lung in sepsis". Dr. Traber reiterated the point presented previously by Dr. Spragg that in sepsis, the lesion that is dominant is a change in pulmonary microvascular permeability with edema formation. The permeability changes are again associated with the release of proteolytic enzymes and oxygen free radicals, either from polymorphonuclear cells or pulmonary macrophages. Dr. Traber pointed out that a majority of the studies done in animal models had

demonstrated the same lesions seen in humans. Most of this work was done in animals who had low cardiac output. His group had developed high cardiac output sepsis. They found with the elevations in outputs, the lung lesion was not as severe. Evidence was presented that this might be the result of a washing of these polymorphonuclear cells from the pulmonary microvasculature, by the increases in blood flow associated with the elevated outputs.

As discussion that followed these presentations would indicate, adult respiratory distress syndrome and other forms of pulmonary microvascular damage associated with trauma and sepsis are commonly associated with deposition of polymorphonuclear cells and the release of mediators. Mediators may also be produced by other phagocytic cells of the lung. Mediators then induce permeability changes in the microvasculature and subsequent leakiness and damage to the pulmonary endothelial type I alveolar cells. This lung damage then leads to the ultimate death of the subject in some 60% of the cases. Those that survive have additional injury resulting from the healing processes that ensue. The mechanisms responsible for the deposition of the cells and the period of time that they remain sequestered in the microcirculation require considerable further study as to the mechanisms and mediators that are responsible.

Shock Society Symposia

SYMPOSIUM III: VASCULAR SMOOTH MUSCLE CONTROL

Co-Chairmen: Robert F. Bond, Ph.D.
Oral Roberts University

Bart Chernow, M.D.
Bethesda Naval Hospital

This symposium entitled "Vascular Smooth Muscle Control" was designed to provide up-to-date information concerning the behavior of vascular smooth muscle during shock and to review the clinical management of the peripheral vasculature of patients in shock.

The first presentation given by Dr. Harvey Sparks, Jr., from Michigan State University, was "Mediation of flow dependent arterial dilation by endothelial cells". In his talk Dr. Sparks provided evidence against the theory of an ascending vasodilation from the microcirculation. He also showed that receptor blockade had no effect on large artery dilation. He contends that variations in blood flow initiate an intimal reaction causing release of a non-prostaglandin metabolite of arachidonic acid which, in turn, stimulates vascular smooth muscle guanylate cyclase leading to increased cyclic GMP and vasodilation.

The second paper given by Dr. Robert Bond from Oral Roberts University was entitled "Intrinsic versus extrinsic regional vascular control during hemorrhagic hypotension and shock". This study, which used data taken from both whole organ and isolated vascular tissue, contrasted the relative importance of autoregulatory and adrenergic nervous system mechanisms in three major vascular beds (i.e., skeletal muscle, cutaneous and mesenteric) during compensatory and decompensatory shock. This author concludes that each vascular bed has its own unique set of control mechanisms which allow independent regulation and down regulation of the adrenergic nervous system during times of stress induced by hemorrhage.

The third paper was presented by Dr. Julian Lombard from the Medical College of Wisconsin and was entitled "Vascular smooth muscle transmembrane potentials during hypotension stress". Dr. Lombard showed that the transmembrane potentials recorded from rat mesenteric veins play an important role in the vascular smooth muscle response to stress. He showed that depolarization occurs during compensation and hyperpolarization occurs during decompensation. These studies emphasized the importance of the venous capacitance vessels during compensation and also suggest that failure of the adrenergic neuroeffector junctions are important in the peripheral vascular failure seen during irreversible shock induced by hemorrhage.

The last two papers given by Drs. Bart Chernow and Bryan Roth from the Bethesda Naval Hospital were entitled "Pharmacological manipulation of the peripheral vasculature in shock states" and "Clinical management of the vasculature in shock states" respectively. These authors emphasize the need for innovative pharmacological approaches to shock reversal. Agents with known efficacy, probable utility and potential usefulness are discussed in detail. A model of factors which modulate α_1 adrenoreceptor function during shock states is also presented.

DISTRIBUTION LIST

Commander
US Army Medical Research and Development Command
ATTN: SGRD-RMS
Fort Detrick, Frederick, Maryland 21701-5012

Defense Technical Information Center (DTIC)
ATTN: DTIC-DDAC
Cameron Station
Alexandria, VA 22304-6145