

AO-A181 050

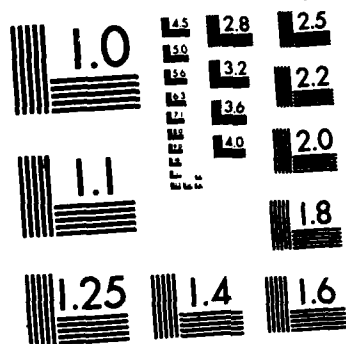
EFFECTS OF ACUTE ACETYLCHOLINESTERASE INHIBITION BY  
PYRIDOSTIGMINE BROMID. (U) LETTERMAN ARMY INST OF  
RESEARCH PRESIDIO OF SAN FRANCISCO CA C E MADE ET AL.  
APR 87 LAIR-235 F/G 6/15

1/1

UNCLASSIFIED

NL





MICROCOPY RESOLUTION TEST CHART  
NATIONAL BUREAU OF STANDARDS-1963-A



2

DTIC FILE COPY

INSTITUTE REPORT NO. 235

EFFECTS OF ACUTE ACETYLCHOLINESTERASE INHIBITION BY  
PYRIDOSTIGMINE BROMIDE INJECTION IN EUVOLEMIC AND  
HYPOVOLEMIC CONSCIOUS SWINE

AD-A181 058

CHARLES E. WADE, PhD  
P.P. WARING, BS  
D.S. TRAIL, BS  
B.F. WILLIAMS, MS  
G.D. BONNER, MBA  
and  
V.L. GILDENGORIN, PhD

DIVISIONS OF MILITARY TRAUMA RESEARCH, COMPARATIVE  
MEDICINE, AND INFORMATION SCIENCES

APRIL 1987

LETTERMAN ARMY INSTITUTE OF RESEARCH  
PRESIDIO OF SAN FRANCISCO, CALIFORNIA 94129

S  
JUN 5 1987  
A

07 6 1 014

Effects of acute acetylcholinesterase inhibition by pyridostigmine  
bromide injection in euvoletic and hypovolemic conscious swine--  
Wade et al

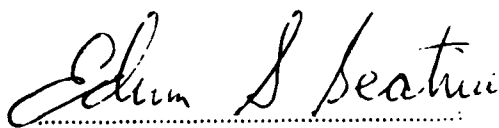
Reproduction of this document in whole or in part is prohibited except with the permission of the  
Commander, Letterman Army Institute of Research, Presidio of San Francisco, California 94129.  
However, the Defense Technical Information Center is authorized to reproduce the document for  
United States Government purposes.

Destroy this report when it is no longer needed. Do not return it to the originator.

Citation of trade names in this report does not constitute an official endorsement or approval of the  
use of such items.

In conducting the research described in this report, the investigation adhered to the "Guide for the  
Care and Use of Laboratory Animals," as promulgated by the Committee on Revision of the Guide  
for Laboratory Animal Facilities and Care, Institute of Laboratory Animal Resources, National  
Research Council.

This material has been reviewed by Letterman Army Institute  
of Research and there is no objection to its presentation and/  
or publication. The opinions or assertions contained herein  
are the private views of the author(s) and are not to be con-  
strued as official or as reflecting the views of the Department  
of the Army or the Department of Defense. (AR 360-5)

 24 Apr 81  
(Signature and date)

This document has been approved for public release and sale; its distribution is unlimited.

UNCLASSIFIED

SECURITY CLASSIFICATION OF THIS PAGE

AD-A181058

## REPORT DOCUMENTATION PAGE

Form Approved  
OMB No 0704-0188  
Exp. Date Jun 30, 1986

1a. REPORT SECURITY CLASSIFICATION <b>UNCLASSIFIED</b>			1b. RESTRICTIVE MARKINGS		
2a. SECURITY CLASSIFICATION AUTHORITY			3. DISTRIBUTION / AVAILABILITY OF REPORT This document has been approved for public release and sale. Unlimited.		
2b. DECLASSIFICATION / DOWNGRADING SCHEDULE			4. PERFORMING ORGANIZATION REPORT NUMBER(S)		
6a. NAME OF PERFORMING ORGANIZATION Letterman Army Institute of Research			6b. OFFICE SYMBOL (if applicable)		7a. NAME OF MONITORING ORGANIZATION US Army Medical Research and Development Command
6c. ADDRESS (City, State, and ZIP Code) Division of Military Trauma Research, LAIR, Presidio of San Francisco, CA 94129-6800			7b. ADDRESS (City, State, and ZIP Code) Fort Detrick, Frederick, MD 21701		
8a. NAME OF FUNDING / SPONSORING ORGANIZATION		8b. OFFICE SYMBOL (if applicable)		9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER	
8c. ADDRESS (City, State, and ZIP Code)		10. SOURCE OF FUNDING NUMBERS			
		PROGRAM ELEMENT NO.	PROJECT NO. A874 3S162772	TASK NO. AB	WORK UNIT ACCESSION NO WU 086
11. TITLE (Include Security Classification) Institute Report No. 235, Effects of Acute Acetylcholinesterase Inhibition by Pyridostigmine Bromide Injection in Euvoletic and Hypovolemic Conscious Swine					
12. PERSONAL AUTHOR(S) C.E. Wade, PhD, P.P. Waring, BS, D.S. Trail, BS, B.F. Williams, MS, G.D. Bonner, MBA, and V.L. Gildengorin, PhD					
13a. TYPE OF REPORT Institute Report		13b. TIME COVERED FROM 1984 TO 1987		14. DATE OF REPORT (Year, Month, Day) 1987 April	
				15. PAGE COUNT 14	
16. SUPPLEMENTARY NOTATION					
17. COSATI CODES			18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)		
FIELD	GROUP	SUB-GROUP	Acetylcholinesterase, Pyridostigmine, Hemorrhage, Swine		
19. ABSTRACT (Continue on reverse if necessary and identify by block number) The effects of acute reduction of blood cholinesterase activity, induced by pyridostigmine bromide injection (300 ug/kg intra-arterially), on physiological and biochemical parameters were assessed in conscious swine with and without hemorrhagic hypotension. Pyridostigmine administration reduced red blood cell acetylcholinesterase (AChE) activity by 61% with values returning to basal values within 3 hrs in both euvoletic and hypotensive animals. In hypovolemic animals plasma AChE activity was reduced by 35% compared to 14% in euvoletic animals. The greater reduction with hypovolemia was due to a 14% decrease during hemorrhage. The acute reduction of AChE activity by pyridostigmine injection in euvoletic and hypovolemic conscious swine did not significantly alter a range of biochemical and physiological parameters. Acute transient symptoms of reduced AChE activity were noted in a few of the hemorrhaged animals.					
20. DISTRIBUTION / AVAILABILITY OF ABSTRACT <input checked="" type="checkbox"/> UNCLASSIFIED/UNLIMITED <input type="checkbox"/> SAME AS RPT <input type="checkbox"/> DTIC USERS			21. ABSTRACT SECURITY CLASSIFICATION <b>UNCLASSIFIED</b>		
22a. NAME OF RESPONSIBLE INDIVIDUAL Charles E. Wade			22b. TELEPHONE (Include Area Code) (415) 561-5816		22c. OFFICE SYMBOL SGRD-UJ-MT

# Abstract

↓  
The effects of acute reduction of blood cholinesterase activity, induced by pyridostigmine bromide injection (~~300 µg/kg intra-arterially~~), on physiological and biochemical parameters were assessed in conscious swine with and without hemorrhagic hypotension. Pyridostigmine administration reduced red blood cell acetylcholinesterase (AChE) activity by 61% with values returning to basal values within 3 hrs in both euvolemic and hypovolemic animals. In hypovolemic animals plasma AChE activity was reduced by 35% compared to 14% in euvolemic animals. The greater reduction with hypovolemia was due to a 14% decrease during hemorrhage. The acute reduction of AChE activity by pyridostigmine injection in euvolemic and hypovolemic conscious swine did not significantly alter a range of biochemical and physiological parameters. Acute transient symptoms of reduced AChE activity were noted in a few of the hemorrhaged animals. ←



On the conventional battlefield many injuries result in hemorrhage (1). An injury caused by conventional weapons plus chemical agents resulting in hemorrhage will probably expose military personnel to chemical agents due to perforation of protective clothing by the missile producing the injury.

Trauma, such as burns and hemorrhagic hypotension, has been shown to reduce blood cholinesterase activity (2-5). These types of injury also may potentiate the actions of cholinergic drugs (6-8). Piscevic et al (9) found that simultaneous hemorrhage and chemical trauma resulted in the death of animals exposed to normally nonlethal doses of the nerve agent sarin. Hemorrhagic hypotension causes a reduction in blood cholinesterase activity, which may potentiate the lethal effects of nerve agents. Thus, the reduction in blood cholinesterase activity incurred during trauma on the battlefield may lead to an increased susceptibility to poisoning by nerve agents. We therefore investigated the physiological and biochemical effects of acute reduction of blood cholinesterase activity induced by pyridostigmine bromide administration in conscious swine with and without hemorrhagic hypotension.

#### Methods

Immature (2- to 3-month-old) Duroc swine (both gilts and barrows) were studied. The animals were purchased from a commercial supplier and housed in the Institute for at least ten days prior to surgery. They were fed a commercial ration (Purina, St Louis, MO) and allowed water ad lib.

After fasting overnight the animals were given a preanesthetic intramuscular injection of 0.08 mg/kg atropine sulfate, 2.2 mg/kg ketamine HCl and 2.2 mg/kg xylazine. Halothane anesthesia was induced using a face mask and maintained with an endotracheal tube. The posterior aorta was catheterized using sterile procedures (10). The catheter was tunneled under the skin and exited on the dorsal surface of the neck. The animals were observed until fully recovered and returned to holding cages. Catheter patency was maintained by flushing at 3- to 4-day intervals with heparin (1000 u/ml) in normal saline.

After 5 to 7 days of postoperative recovery each animal was fasted overnight. The following morning the animals were transported to the laboratory in a portable holding cage, and they remained in the holding cage. The animals were then connected to a 12-inch pressure-monitoring injection line that had been fitted with a three-way stopcock and filled with heparinized saline. The system was then flushed with heparinized saline and connected to a pressure transducer and monitoring system (Gould, 22405). Following a 30 minute equilibration period, the animals were hemorrhaged at 36 ml/kg, 50% of the estimated blood volume, in a logarithmic fashion (11, 12). Between minutes 0 and 60, equal increments of blood were withdrawn at 9, 19, 44, and 60 min. Upon completion of the hemorrhage the animals received an intra-arterial injection of normal saline (0.1 ml/kg, 0.9% NaCl), n=6 [data from these animals have been reported previously (12)] or pyridostigmine bromide (300 µg/kg, Mestinon® 5 mg/ml, Roche Laboratories, Nutley, NJ) n=7. Additionally, nine (n=9) animals which did not undergo hemorrhage were treated with the same dose of pyridostigmine bromide.

Measurements of hemodynamic variables were obtained at 0, 60, 62, 65, 75, 90, 105, 120, 135, 150, 165, 180, 210, and 240 minutes. Arterial blood samples were taken at 0, 60, 62, 65, 75, 90, 105, 120, 180, and 240 minutes. Additional blood samples were obtained during hemorrhage to determine acetylcholinesterase activity (see Fig. 1). Blood pressure, heart rate, and pulse pressure were measured for one minute prior to each sampling period and an average obtained. Plasma lactate (Sigma Chemical Co., St Louis, MO) and glucose (Beckman Instruments, Anaheim, CA) levels were measured by standard assay techniques. Hematocrit was measured by the microcapillary method. Blood gases were measured by a System 1303, (Instrumentation Laboratory, Lexington, MA). Acetylcholinesterase activities of the plasma and red blood cells were determined with a Technicon Auto Analyzer II system using a modification of the method of Ellman et al (13) adapted by Levine et al (14). Acetylthiocholine was used as the substrate (see Letterman Army Institute of Research Standard Operating Procedure OP-ACH-38, Auto Analyzer II Acetylcholinesterase Assay, 1982).

Data were analyzed using a two-way analysis of variance with comparisons made between groups and over time. Differences between means were assessed using the Newman-Keuls procedure. A significance level of 0.05 was



used on all tests. Values in the text are mean plus or minus the standard error of the mean.

### Results

**Hemodynamic:** Heart rate was not altered during the sampling periods by hemorrhage or the administration of pyridostigmine (Table I). In euvolemic animals blood pressure was not altered by pyridostigmine; however, pulse pressure was significantly decreased by 12 mmHg. Blood pressure was reduced by hemorrhage and was not affected by injection of pyridostigmine.

**Arterial Blood Gases:** Arterial blood measurements were not altered in euvolemic animals by the injection of pyridostigmine (Table II). There were differences in arterial  $O_2$  pressure and  $HCO_3$  between the two groups of hemorrhaged animals, but these differences were not altered by pyridostigmine administration because a time group interaction was not noted. Thus, pyridostigmine did not change arterial blood gas in euvolemic and hemorrhaged animals.

**Lactate/Glucose/Hematocrit:** Although blood lactate and glucose levels increased during hemorrhage and hematocrit decreased, no effect from pyridostigmine administration was noted (Table III). Also in euvolemic animals no changes were noted due to this drug dosage.

**Acetylcholinesterase Activity:** Administration of pyridostigmine caused an immediate reduction in plasma and red blood cell AChE activity in both euvolemic and hemorrhaged animals (Table IV). Red blood cell AChE activity was acutely reduced (more than 50%) and gradually returned to basal levels over the following three hours (Fig. 1). In euvolemic animals given pyridostigmine, a 14% decrease in plasma AChE activity occurred, while in hemorrhaged animals a 35% reduction was noted. This difference was due to a 15% decrement in activity incurred over the course of hemorrhage.

**Adverse Effects:** Although few of the biochemical and physiological measurements were altered by pyridostigmine administration, side effects were noted. The side effects of pyridostigmine occurred only in the hemorrhaged animals. Upon administration of pyridostigmine following hemorrhage, a pronounced bradycardia was observed in 4 of 7 animals (Fig. 2). This bradycardia was rectified within

two minutes as there was no difference in heart rate or that of hemorrhage-control animals. In two animals hemorrhaged and given pyridostigmine, fasciculation was observed, and in one of these animals a period of labored breathing was noted. No adverse effects were noted in euvolemic animals treated with pyridostigmine.

### Discussion

Pyridostigmine is a reversible inhibitor of acetylcholinesterase (AChE), the enzyme that degrades the neurotransmitter acetylcholine. In the present study pyridostigmine was used to evaluate the effects of acute reductions of AChE activity in hemorrhaged swine. Hemorrhage and trauma reduce AChE activity (2-5), which may be detrimental to individuals exposed to further reductions in activity, thus potentiating the actions of acetylcholine. In the present study the biochemical and physiological effects of further reductions in AChE activity following hemorrhage were investigated and no pronounced decrements noted. Furthermore, in euvolemic animals the reduction of AChE activity showed no effect.

The absence of changes in cardiovascular and biochemical parameters in the presence of reductions of 33% in plasma and 61% in red blood cell AChE activity may be due to the preponderance of AChE in tissues. In fact, a reduction of over 90% in blood activity is often required to elicit symptoms of acetylcholinesterase poisoning (15, 16).

Symptoms of acetylcholine toxicity (bradycardia, fasciculation, labored breathing) were noted in hemorrhaged animals following reduction of AChE activity induced by pyridostigmine administration. Though the symptoms were acute and inconsistent in this group, they are pronounced in that no adverse responses were noted in either of the other treatment groups, hemorrhage untreated or euvolemia with pyridostigmine. The presence of symptoms following pyridostigmine administration to hypotensive animals in the present study are in conflict with the observations of Piscevic et al (9). In their studies simultaneous hemorrhage and reduction of AChE activity by administration of a nonlethal dose of the nerve agent sarin to rats resulted in death with symptoms not observed or of "insignificant" intensity. Although symptoms were noted in the present study of swine, all animals survived the procedure, and the reduction in AChE

activity by pyridostigmine administration was probably not as pronounced as that induced by sarin.

In conclusion, acute reduction of AChE activity by pyridostigmine administration in euvoletic or hemorrhagic conscious swine failed to significantly alter a range of biochemical and physiological parameters. However, acute transient symptoms of reduced AChE activity were noted in a few of the hemorrhaged animals.

#### Recommendations

1. Further work is required to study the combined effects of trauma and exposure to nerve agents.
2. Future work should be conducted in an animal model that allows symptomatology as well as physiological and biochemical parameters to be assessed.

### References

1. Bellamy RF. The causes of death in conventional land warfare: implications for combat casualty care research. *Milit Med* 1984;149:55-62.
2. Assur MV, Ermakov AM. A change of blood cholinesterase activity in acute blood loss. *Patol Fiziol Eksp Ter* 1968;12:16-18.
3. Frawley JP, Artz CP, Howard JM. A study of plasma and erythrocyte cholinesterase activity in combat casualties. In: Howard JM ed. *The systemic response to injury*; vol 1. Washington, DC: Walter Reed Army Medical Center, 1956:261-267.
4. Viby-Mogensen J, Hanel HK, Hansen E, Sorensen B, Grace J. Serum cholinesterase activity in burned patients. I: Biochemical findings. *Acta Anaesthesiol Scand* 1975;19:159-168.
5. Wade CE, Waring PP, Gildengorin VL, Trail DS, Williams BF, Bonner GD, DeJong RH. Acetylcholinesterase activity of plasma and erythrocytes during hemorrhage in conscious swine. Presidio of San Francisco, California: Letterman Army Institute of Research (in press).
6. Whittaker M. Plasma cholinesterase variants on the anaesthetist. *Anaesthesia* 1980; 35:174-197.
7. Sunew KY, Hicks RG. Effects of neostigmine and pyridostigmine on duration of succinylcholine action and pseudocholinesterase activity. *Anesthesiology* 1978;49:188-191.
8. Viby-Mogensen J, Hanel HK, Hansen E, Grace J. Serum cholinesterase activity in burned patients. II: Anaesthesia, suxamethonium, and hyperkalaemia. *Acta Anaesthesiol Scand* 1975;19:169-179.
9. Piscevic S, Vojvodic V, Duknic M. Reciprocal effect of sarin and mechanical injury with loss of blood on survival of experimental animals. *Vojnosanit Pregl* 1972;29:155.
10. Traverso LW, Moores CC, Tillman FJ. A clinically applicable exsanguination shock model in swine. *Circ Shock* 1984;12:1-7.

11. Hannon JP, Jennings PB Jr, Dixon RS. Physiologic aspects of porcine hemorrhage. II: Alterations in heart rate and arterial pressure during fifty percent blood volume loss in the conscious animal. Presidio of San Francisco, California: Letterman Army Institute of Research, 1981; Institute Report No. 94.
12. Wade CE, Waring PP, Trail DS, Williams BF, Bonner GD, Gildengorin VL. Effects of atropine, 2-PAM, or pyridostigmine on responses to hemorrhage in conscious swine. Presidio of San Francisco, Letterman Army Institute of Research (in press).
13. Ellman GL, Courtney KD, Andres V, Featherstone RM. A new and rapid colorimetric determination of acetylcholinesterase activity. Biochem Pharmacol 1961;7:88-95.
14. Levine JB, Scheidt RA, Nelson JA. An automated micro-determination of serum cholinesterase. In: Skeggs LT, ed. Automation in analytical chemistry. Technician Symposia 1965. New York: Medical Inc., 1966:582-585.
15. Koelle GB. Neurohumoral transmission and the autonomic nervous system. In: Goodman LS, Gilman A, eds. The pharmacological basis of therapeutics. 5th ed. New York: MacMillan Publishing Co., 1976:404-444.
16. Koelle GB. Anticholinesterase agents. In: Goodman LS, Gilman A, eds. The pharmacological basis of therapeutics. 5th ed. New York: MacMillan Publishing Co., 1976:445-476.

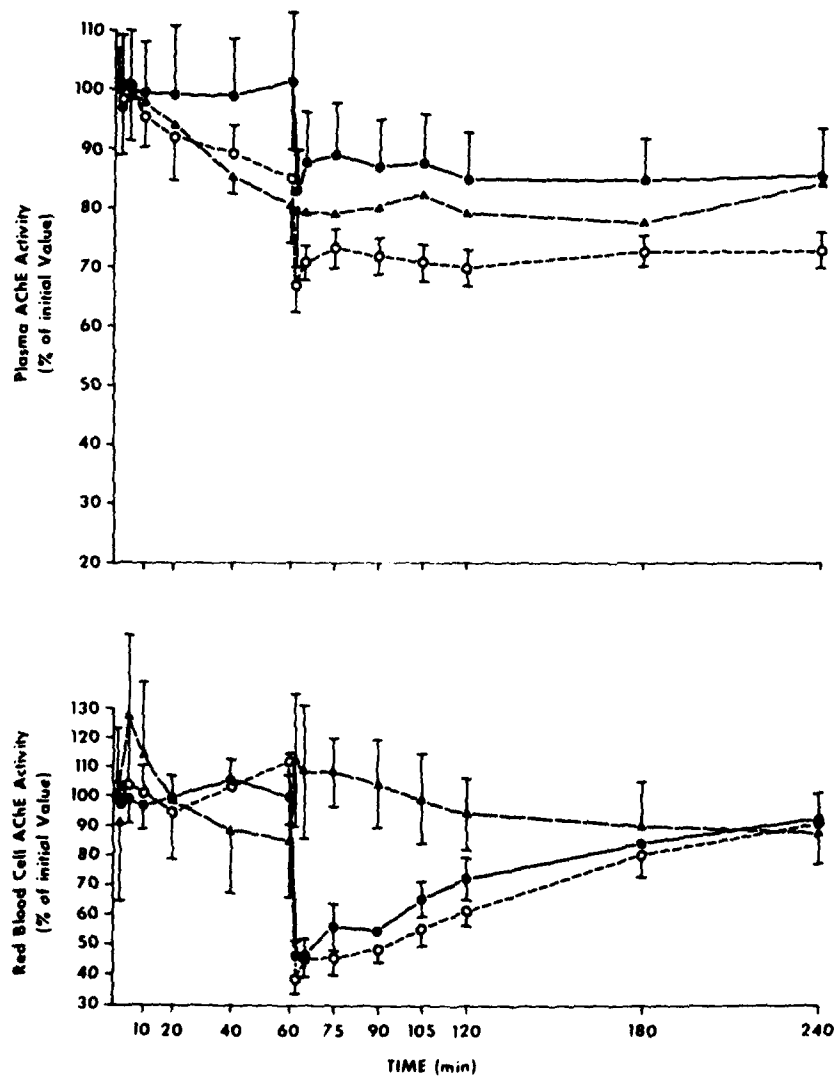


Fig 1: Red blood cell and plasma acetylcholinesterase activity (AChE), as a percent of initial activity, in hemorrhage-control (▲—▲), (for initial values, see Table IV), hemorrhage-pyridostigmine (○—○), and control-pyridostigmine (●—●) conscious swine.

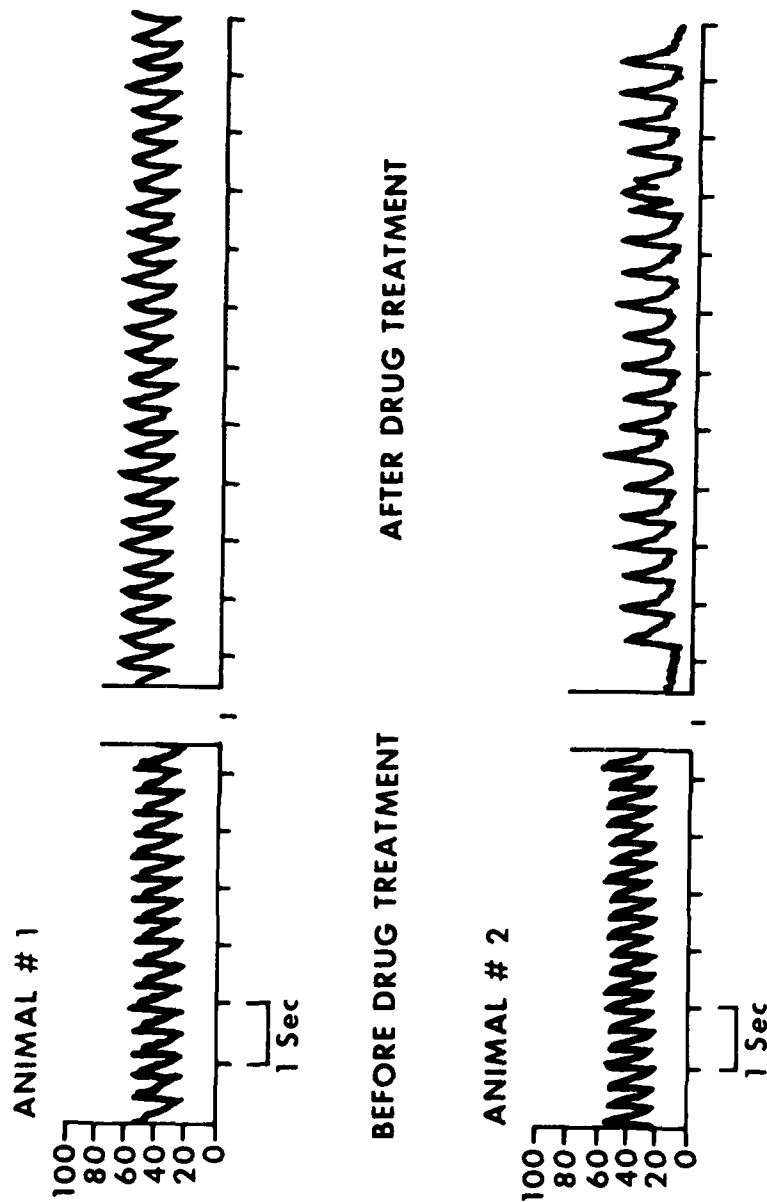


Fig 2: Blood pressure tracing in three animals prior to and immediately following intra-arterial injection of pyridostigmine (33  $\mu$ g/kg).

Table 1: Hemodynamic Responses

	0	50	62	65	75	90	105	120	135	150	165	180	210	240
Heart Rate (b/min)														
Hemorrhage- Saline	141±5	133±12	121±10	116±9	123±11	136±13	132±11	141±12	143±6	141±8	150±9	162±5	148±5	167±11
Hemorrhage- Pyridox	135±6	149±12	132±8	127±7	126±12	136±13	140±13	144±16	156±14	154±18	151±11	147±12	150±12	150±11
Control- Pyridox	130±5	133±9	130±8	127±6	131±6	127±6	125±4	127±4	131±4	120±5	135±6	137±6	133±4	120±5
Mean Arterial Pressure (mmHg)														
Hemorrhage- saline	96±5	36±3	39±4	46±6	45±5	41±2	56±4	44±4	56±5	52±2	62±8	49±4	57±5	56±4
Hemorrhage- pyridox	95±5	41±5	46±5	48±5	52±7	46±7	49±6	52±6	55±6	46±5	56±8	54±5	63±3	46±6
Control- pyridox	98±3	94±4	96±4	97±3	94±4	89±4	95±4	94±2	89±5	89±4	85±5	89±4	86±3	91±4
Pulse Pressure (mmHg)														
Hemorrhage- Saline	53±7	39±7	45±8	34±3	44±10	42±8	49±13	52±12	48±11	48±12	37±4	46±14	43±13	56±19
Hemorrhage- Pyridox	53±4	31±3	32±4	35±4	37±4	37±4	36±4	46±4	39±4	35±4	36±4	46±4	36±4	35±3
Control- Pyridox	56±2	53±3	53±3	56±3	57±4	54±4	52±4	53±4	45±4	46±4	42±4 <sup>o</sup>	56±3	45±4	44±4

<sup>a</sup>: significantly different from the 60 min pre-injection value



Table II: Arterial Blood Gases

	0	Time (min)									
		5	10	15	20	25	30	35	40	45	50
$\text{PO}_2$ (mmHg)											
Hemorrhage-Control	982.3	1243.5	1155.5	1143.3	1125.5	1073.9	1175.6	1083.6	1092.6	1213.8	1213.8
Hemorrhage-Pyridox	853.3 <sup>†</sup>	1012.8 <sup>†</sup>	912.7 <sup>†</sup>	923.3 <sup>†</sup>	925.4 <sup>†</sup>	913.4 <sup>†</sup>	892.4 <sup>†</sup>	882.4 <sup>†</sup>	963.4 <sup>†</sup>	913.3 <sup>†</sup>	913.3 <sup>†</sup>
Control-Pyridox	922.3	832.3	802.3	902.3	802.4	872.2	912.2	892.3	872.3	942.3	942.3
$\text{PCO}_2$ (mmHg)											
Hemorrhage-Control	372.1	282.2	312.2	302.2	312.1	322.1	332.2	302.1	352.1	322.1	322.1
Hemorrhage-Pyridox	362.1	312.1	342.3	332.1	322.1	322.1	322.1	352.1	352.2	352.1	352.1
Control-Pyridox	402.1	302.1	302.1	302.1	402.1	302.1	302.1	302.1	402.1	302.1	302.1
$\text{HCO}_3^-$											
Hemorrhage-Control	252.1	202.1	212.1	202.1	202.1	212.1	222.1	232.1	242.1	242.1	242.1
Hemorrhage-Pyridox	272.1 <sup>†</sup>	252.1 <sup>†</sup>	242.1 <sup>†</sup>	232.2 <sup>†</sup>	232.2 <sup>†</sup>	232.1 <sup>†</sup>	232.1 <sup>†</sup>	252.1 <sup>†</sup>	262.1 <sup>†</sup>	262.1 <sup>†</sup>	262.1 <sup>†</sup>
Control-Pyridox	282.2	272.1	272.1	272.1	272.1	272.1	272.1	262.1	262.1	272.1	272.1
pH											
Hemorrhage-Control	7.4329.01	7.4629.02	7.4229.02	7.4229.01	7.4129.01	7.4229.01	7.4329.01	7.4329.01	7.4229.02	7.4829.02	7.4829.02
Hemorrhage-Pyridox	7.5029.01	7.5029.02	7.4729.03	7.4629.03	7.4529.03	7.4529.03	7.4729.03	7.4529.03	7.4629.03	7.4729.02	7.4729.02
Control-Pyridox	7.4829.01	7.4829.01	7.4829.02	7.4829.01	7.4829.01	7.4729.01	7.4829.01	7.4529.01	7.4529.01	7.4629.01	7.4629.01

<sup>†</sup>: significantly different from hemorrhage-control, p < 0.05.

Table III: Lactate/Glucose/Hematocrit

		Time (min)								
		60	62	65	75	90	105	120	180	240
Lactate (mg/dL)										
Hemorrhage-Control	921	56215	63212	60210	61213	50212	52211	53211	27219	22219
Hemorrhage-Pyridox	721	32216	42218	47219	52219	50210	44217	34219	24217	18217
Control-Pyridox	621	822	822	821	621	521	621	621	621	521
Glucose (mg/dL)										
Hemorrhage-Control	8927	145224	157216	163228	162219	150220	138221	151221	129210	123210
Hemorrhage-Pyridox	107217	120218	150217	160226	177222	150218	153213	136213	144217	130215
Control-Pyridox	80216	83218	83218	96218	87219	92218	90210	91219	95211	96219
Hematocrit (%)										
Hemorrhage-Control	2722	2321	2321	2322	2221	2322	2222	2222	2222	2121
Hemorrhage-Pyridox	2721	2221	2321	2422	2222	2221	2222	2222	2222	2222
Control-Pyridox	2621	2521	2621	2621	2621	2621	2521	2521	2521	2521

Table IV: Acetylcholinesterase Activity

Plasma AChE (u/ml)	Time (min)									
	0	15	30	45	60	75	90	105	120	135
<b>Hamorrhage-Saline</b>										
0.5020.01	0.4020.02	0.4020.02	0.3020.02	0.3020.02	0.4020.02	0.3020.02	0.4020.02	0.4120.02	0.3020.02	0.3020.03
<b>Hamorrhage-Pyridine</b>										
0.4120.02	0.3020.01	0.2720.02	0.2020.01	0.3020.01	0.2020.01	0.3020.01	0.2020.01	0.2020.01	0.2020.01	0.3020.01
<b>Control-Pyridine</b>										
0.4220.05	0.4320.05	0.3020.03	0.3720.04	0.3720.04	0.3720.03	0.3720.04	0.3720.03	0.3720.03	0.3020.03	0.3020.03
<b>Red Blood Cell AChE (u/ml P<sub>50</sub>)</b>										
<b>Hamorrhage-Saline</b>										
4.1120.00	3.4720.79	4.5320.00	4.3020.03	4.4120.43	4.2320.02	4.0120.05	3.0020.40	3.0020.04	3.5020.37	
<b>Hamorrhage-Pyridine</b>										
3.8320.30	4.0020.50	1.5420.10	1.8020.10	1.0420.10	1.0120.10	2.2320.20	2.4120.10	3.2120.27	3.5020.30	
<b>Control-Pyridine</b>										
4.0120.30	4.0020.30	2.1420.31	2.2020.33	2.7320.40	2.0020.30	3.1520.20	3.5320.32	4.1220.33	4.4120.32	

\* significantly different from hemorrhage-saline, P&lt;0.05.

\* significantly different from pre-saline value in control-pyridine, P&lt;0.05.

OFFICIAL DISTRIBUTION LIST

Commander  
US Army Medical Research  
and Development Command  
ATTN: SGRD-RMS/Mrs. Madigan  
Fort Detrick, MD 21701-5012

Defense Technical Information Center  
ATTN: DTIC/DDAB (2 copies)  
Cameron Station  
Alexandria, VA 22304-6145

Office of Under Secretary of Defense  
Research and Engineering  
ATTN: R&AT (E&LS), Room 3D129  
The Pentagon  
Washington, DC 20301-3080

The Surgeon General  
ATTN: DASG-TLO  
Washington, DC 20310

HQ DA (DASG-ZXA)  
WASH DC 20310-2300

Commandant  
Academy of Health Sciences  
US Army  
ATTN: HSHA-CDM  
Fort Sam Houston, TX 78234-6100

Uniformed Services University  
of Health Sciences  
Office of Grants Management  
4301 Jones Bridge Road  
Bethesda, MD 20814-4799

US Army Research Office  
ATTN: Chemical and Biological  
Sciences Division  
PO Box 12211  
Research Triangle Park, NC 27709-2211

Director  
ATTN: SGRD-UWZ L  
Walter Reed Army Institute  
of Research  
Washington, DC 20307-5100

Commander  
US Army Medical Research Institute  
of Infectious Diseases  
ATTN: SGRD-UIZ A  
Fort Detrick, MD 21701-5011

Commander  
US Army Medical Bioengineering  
Research & Development Laboratory  
ATTN: SGRD-UBG-M  
Fort Detrick, Bldg 568  
Frederick, MD 21701-5010

Commander  
US Army Medical Bioengineering  
Research & Development Laboratory  
ATTN: Library  
Fort Detrick, Bldg 568  
Frederick, MD 21701-5010

Commander  
US Army Research Institute  
of Environmental Medicine  
ATTN: SGRD-UE-RSA  
Kansas Street  
Natick, MA 01760-5007

Commander  
US Army Institute of Surgical Research  
Fort Sam Houston, TX 78234-6200

Commander  
US Army Research Institute  
of Chemical Defense  
ATTN: SGRD-UV-AJ  
Aberdeen Proving Ground, MD 21010-5425

Commander  
US Army Aeromedical Research Laboratory  
Fort Rucker, AL 36362-5000

AIR FORCE Office of Scientific  
Research (NL)  
Building 410, Room A217  
Bolling Air Force Base, DC 20332-6448

Commander  
USAFSAM/TSZ  
Brooks Air Force Base, TX 78235-5000

Head, Biological Sciences Division  
OFFICE OF NAVAL RESEARCH  
800 North Quincy Street  
Arlington, VA 22217-5000

END

7-87

DTIC