

NO-A143 007

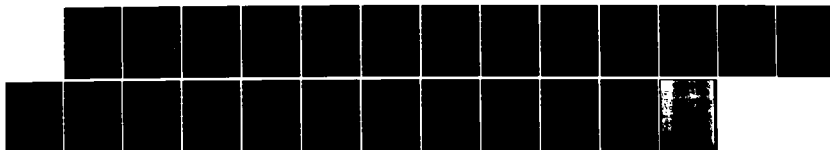
FLUID REPLACEMENT DURING HYPOTHERMIA(U) ARMY RESEARCH
INST OF ENVIRONMENTAL MEDICINE NATICK MA
D E ROBERTS ET AL. 02 MAR 84 USARIEN-M16/84

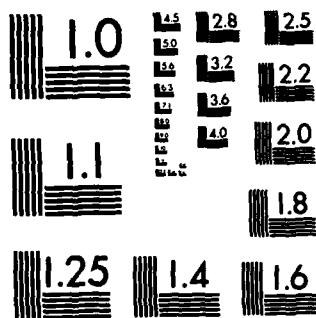
1/1

UNCLASSIFIED

F/G 6/16

NL





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

AD-A143 807

DTIC FILE COPY

UNCLASSIFIED
SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

REPORT DOCUMENTATION PAGE		READ INSTRUCTIONS BEFORE COMPLETING FORM
1. REPORT NUMBER M16/84	2. GOVT ACCESSION NO. AD-A143 807	3. RECIPIENT'S CATALOG NUMBER
4. TITLE (and Subtitle) Fluid Replacement During Hypothermia		5. TYPE OF REPORT & PERIOD COVERED
7. AUTHOR(s) D. E. Roberts; J. G. Barr; D. Kerr; C. Murray; and R. Harris		6. PERFORMING ORG. REPORT NUMBER
9. PERFORMING ORGANIZATION NAME AND ADDRESS US Army Research Institute of Environmental Medicine, Natick, MA 01760		8. CONTRACT OR GRANT NUMBER(s)
11. CONTROLLING OFFICE NAME AND ADDRESS Same		10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS
14. MONITORING AGENCY NAME & ADDRESS (if different from Controlling Office) US Army Medical Research & Development Command, Washington, DC 20314		12. REPORT DATE 2 March 1984
		13. NUMBER OF PAGES
		15. SECURITY CLASS. (of this report) Unclassified
		15a. DECLASSIFICATION/DOWNGRADING SCHEDULE
16. DISTRIBUTION STATEMENT (of this Report) Distribution of this document is unlimited.		
17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report) DTIC ELECTE AUG 3 1984		
18. SUPPLEMENTARY NOTES A		
19. KEY WORDS (Continue on reverse side if necessary and identify by block number) Plasma volume, contractility, hematocrit, cardiac output		
20. ABSTRACT (Continue on reverse side if necessary and identify by block number) Hypothermia produces acidosis, depressed cardiac function, hypovolemia and hypertension. This study was designed to examine the cardiovascular dynamics involved with restoration of the hypovolemia before rewarming. Mixed breed splenectomized adult dogs (n=16) were anesthetized with pentobarbital and cooled to a right atrial temperature of 25°C at a rate of 3°C/Hr. The animals were maintained at 25°C for 6 hours and rewarmed at 3°C/Hr. One group (1) was given no fluid, one group (2) was given saline (20% of plasma		

DD FORM 1473

EDITION OF 1 NOV 65 IS OBSOLETE

UNCLASSIFIED

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

84 08 1 061

UNCLASSIFIED

SECURITY CLASSIFICATION OF THIS PAGE(When Data Entered)

volume infused in 10 min.) two hours after reaching 25°C and one group (3) received saline just prior to rewarming. The hematocrit was elevated in all groups ($P \leq 0.05$) upon cooling, but did not differ between groups even after saline was given. Cardiac output (CO) at 25°C was 35% of precooled values. The second group increased their CO by 15% with fluid and this CO was maintained higher than groups 1 or 3 for the next four hours. Plasma volume, heart rate, and cardiac contractility returned to control levels upon rewarming, but CO remained low ($\leq 10\%$). The level of CO at the start of rewarming did not affect the final level of CO.

UNCLASSIFIED

SECURITY CLASSIFICATION OF THIS PAGE(When Data Entered)

FLUID REPLACEMENT DURING HYPOTHERMIA

D. E. Roberts, J. G. Barr, D. Kerr,
C. Murray and R. Harris

US Army Research Institute of Environmental Medicine

Natick, MA 01760



A1

ABSTRACT

Hypothermia produces acidoses, depressed cardiac function, hypovolemia and hypotension. This study was designed to examine the cardiovascular dynamics involved with restoration of the hypovolemia before rewarming. Mixed breed splenectomized adult dogs (n=16) were anesthetized with pentobarbital and cooled to a right atrial temperature of 25°C at a rate of $3^{\circ}\text{C}/\text{Hr}$. The animals were maintained at 25°C for 6 hours and rewarmed at $3^{\circ}\text{C}/\text{Hr}$. One group (1) was given no fluid, one group (2) was given saline (20% of plasma volume infused in 10 min.) two hours after reaching 25°C and one group (3) received saline just prior to rewarming. The hematocrit was elevated in all groups ($P < 0.05$) upon cooling, but did not differ between groups even after saline was given. Cardiac output (CO) at 25°C was 35% of precooled values. The second group increased their CO by 15% with fluid and this CO was maintained higher than groups 1 or 3 for the next four hours. Plasma volume, heart rate, and cardiac contractility returned to control levels upon rewarming, but CO remained low ($< 10\%$). The level of CO at the start of rewarming did not affect the final level of CO.

Plasma volume, contractility, hematocrit, cardiac output

INTRODUCTION

One of the major problems in treating hypothermic victims is knowing and understanding what physiological changes are occurring and to what extent they are self reversible and what must be treated. As body temperature drops, blood viscosity increases (14) with resulting changes in pressure-flow relationships (11). Volume shifts, electrolyte changes and acid-base changes are also consequences of lowered body temperature.

Chen (3) has reported that the elevated blood viscosity at 25°C is due to three factors; hemoconcentration, the low temperature, and the low flow state. Chen reported that changes in hematocrit without changes in temperature result in a 10% increase in viscosity. Decreasing the body temperature to 25°C increases the viscosity by another 13% while lowering cardiac output or decreasing the shear rate increases the viscosity by 39%. Kanter (8) has reported that dogs without spleens still increase their hematocrit by 7.8% during hypothermia.

Nose (13) reported that the changes in hemodynamics resulted in changes in plasma volume. The changes in compliances of vascular and interstitial spaces are due to closure of the peripheral circulation and redistribution of blood. Barbour (1) reported that lowered body temperature resulted in depression of the hypothalamus which abolished some reflexes allowing an increase in extracellular fluid.

The aim of this study was to examine the effects of cold on fluid volumes and cardiovascular dynamics during hypothermia. We also were interested in what changes in these parameters could be affected by administration of normal saline in bolus form during the hypothermia and just prior to rewarming.

METHODS.

Sixteen healthy mongrel dogs were used for this study. The weights ranged from 15 Kg to 21 Kg. The animals were divided into 3 groups: group 1 received no fluid, group 2 received saline (20% of plasma volume) 4 hours before rewarming, and group 3 received saline (20% of plasma volume) just before rewarming. Animals were prepared for hypothermia by surgically removing the spleen and implanting a Konigsberg pressure transducer in the left ventricular chamber. At least two weeks were allowed between surgery and the induction of hypothermia.

On the day of the experiment, the animal was anesthetized with sodium pentobarbitol (25mg/Kg) and a trachea tube inserted. The hair from the entire body was clipped to facilitate cooling. Arterial pressure was measured from the right femoral artery by either a Statham P-23 AA strain gauge or a Millar catheter-tip pressure transducer. Right atrial pressure was measured by a catheter connected to a Statham P-23 BB advanced to a level just above the right atrium. All pressures were recorded on a Brush 200 8-channel recorder.

Cardiac output was measured by dye dilution using Cardro-green dye. Dye (2.5mg) was injected into the right atrium via

the external jugular vein and arterial blood was withdrawn from the left femoral artery (40cc/min.) and passed through a Lexington Instruments Clinical Densitometer. The output curve was recorded on a Gilson recorder and later digitized and entered into a Digital Equipment PDP-11 for calculation according to the standard methods.

An ECG was attached and lead II was used to obtain heart rate and for detection of abnormal cardiac rhythms. Ventricular pressure was recorded from the Konigsberg pressure transducer in the left ventricle and later analyzed as an index of contractility (6).

Temperatures were obtained from thermocouples attached to the skin and cardiac temperature was obtained from a thermocouple advanced down the external jugular vein and stopped just above the heart. Temperatures were measured by a Leeds and Northrup Numatron Scanning facility and recorded on a Digital Equipment PDP-11 computer. Each temperature was printed every 60 seconds.

Plasma volume was obtained by a dye dilution method using Evans blue dye injected into the right atrium and samples withdrawn from the femoral artery. Arterial blood was withdrawn from the right femoral artery for blood gas determination by a Radiometer ABL-2. Hematocrit determinations were made on arterial blood.

Cooling and rewarming (at a rate not greater than $3^{\circ}\text{C}/\text{Hr}$) was performed by an Omitherm unit circulating fluid through blankets situated above and below the animal.

Most measurements were recorded continuously, but all are reported for the following intervals: pre-cool (Stage 1), 25°C (Stage 2), 25°C-6 Hrs, (Stage 3) and rewarm (Stage 4). Animals were respiration only if they did not respire on their own.

RESULTS

Figure 1 shows the changes in plasma volume for the three different groups over the time course of the hypothermia. There

Figure 1

was no significant difference in the plasma volumes of the three groups in the pre-cool or control phase. Volumes measured after reaching 25°C are all significantly lower ($P < .05$) than control levels. Comparison of volumes within groups across the 6 Hrs at 25°C indicates no change in the group receiving no fluid and in the group receiving fluid before rewarming. The group receiving fluid 4 Hrs prior to rewarming shows an increase in volume, but it is not statistically different. The plasma volumes measured after rewarming are not significantly different from the pre-cool values for any group.

Figure 2

Figure 2 shows the change in hematocrit for all groups across all phases of the study. The hematocrit in each group is elevated upon cooling and also when rewarmed.

Table 1. Mean values for blood parameters

	Stage	Group 1	Group 2	Group 3
(Na ⁺) mEq/L	1	149.3 $\pm$ 1.0	148.4 $\pm$ 1.1	152.6 $\pm$ 3.0
	2	147.5 $\pm$ 1.8	149.4 $\pm$ 1.0	153.7 $\pm$ 5.5
	3	148.4 $\pm$ 1.3	149.6 $\pm$ 2.2	151.5 $\pm$ 3.2
	4	147.2 $\pm$ 2.7	150.7 $\pm$ 2.6	147.4 $\pm$ 4.0
(K ⁺) mEq/L	1	3.7 $\pm$ 0.1	3.8 $\pm$ 0.2	3.7 $\pm$ 0.2
	2	3.5 $\pm$ 0.2	3.3 $\pm$ 0.1	3.4 $\pm$ 0.2
	3	3.5 $\pm$ 0.2	3.4 $\pm$ 0.3	3.6 $\pm$ 0.2
	4	3.3 $\pm$ 0.2	4.1 $\pm$ 0.2	3.6 $\pm$ 0.2
pO ₂	1	70.7 $\pm$ 3.9	83.6 $\pm$ 4.2	72.9 $\pm$ 3.9
	2	32.3 $\pm$ 3.2	30.2 $\pm$ 1.7	43.7 $\pm$ 5.5
	3	38.1 $\pm$ 5.3	39.1 $\pm$ 5.8	47.8 $\pm$ 5.2
	4	81.6 $\pm$ 4.0	90.0 $\pm$ 1.7	88.9 $\pm$ 3.7
pCO ₂	1	49.1 $\pm$ 1.8	46.3 $\pm$ 1.0	53.1 $\pm$ 2.9
	2	55.4 $\pm$ 2.9	63.1 $\pm$ 0.8	59.1 $\pm$ 4.1
	3	62.5 $\pm$ 3.3	65.4 $\pm$ 5.2	63.8 $\pm$ 3.0
	4	38.5 $\pm$ 3.5	38.5 $\pm$ 0.6	38.4 $\pm$ 1.2
pH	1	7.162 $\pm$.02	7.190 $\pm$.03	7.200 $\pm$.03
	2	7.122 $\pm$.03	7.010 $\pm$.03	7.130 $\pm$.02
	3	7.006 $\pm$.02	7.040 $\pm$.04	7.110 $\pm$.02
	4	7.214 $\pm$.01	7.180 $\pm$.05	7.290 $\pm$.02

The blood electrolyte changes, pH, and blood gas changes are shown in Table 1. There is no difference for plasma Na⁺ across groups or across phases. The plasma K⁺ tends to drop during hypothermia and tends to rebound during rewarming. The values for the blood gases indicate that the animals are anoxic with elevated pCO₂, lowered pO₂ and lowered pH. This pattern is consistent with depressed respiration following administration of pentobarbital for the initial surgery.

Table 2. Mean values for urinary parameters

	Stage	Group 1	Group 2	Group 3
(Na+) mEq/L	1	192.7 + 38.9	182.4 + 21.3	165.9 + 48.4
	2	111.2 + 17.5	139.4 + 14.1	116.3 + 34.9
	3	70.6 + 19.6	121.0 + 19.5	91.8 + 40.6
	4	56.0 + 21.0	120.2 + 24.9	84.7 + 30.0
(K+) mEq/L	1	103.6 + 19.3	89.9 + 07.9	92.0 + 18.8
	2	170.2 + 29.9	157.2 + 25.2	167.7 + 39.5
	3	143.7 + 41.2	149.3 + 27.9	188.6 + 9.7
	4	126.7 + 33.2	180.6 + 41.6	168.1 + 24.4
OSM	1	1497.5 + 144.0	1417.4 + 159.1	1353.8 + 110.9
	2	1363.0 + 144.1	1050.8 + 131.7	948.8 + 77.1
	3	928.6 + 104.1	842.5 + 131.1	1144.7 + 101.8
	4	1028.8 + 142.6	982.6 + 161.6	1036.2 + 77.1
Volume	1	21.9 + 9.1	19.2 + 5.3	8.9 + 2.2
	2	12.9 + 2.7	6.2 + 1.3	11.4 + 3.2
	3	7.7 + 3.5	5.4 + 1.7	3.7 + 1.6
	4	5.1 + 1.5	3.8 + 1.2	9.0 + 3.1

Table 2 shows the data for urine for the three groups for the 4 phases. The excretion of Na^+ is lessened for each stage of cooling. The excretion of K^+ is increased for stages 2, 3, and 4 when compared to baseline levels. The volume of urine excretion decreases over the four stages for all groups, but the osmolarity decreases. The lessened osmolarity results from reduced excretion of Na^+ (increased plasma retention) and elevated K^+ (sodium-potassium exchange in the renal excretory mechanism). There is no statistical difference in urinary values for the groups receiving fluid when compared to those not receiving fluid.

The cardiovascular changes occurring during the hypothermia are detailed in Figures 3, 4, and 5 and in Table 3. Figure 3

Figure 3

shows the change in heart rate for the three groups calculated as a percent of baseline levels. The heart rate is significantly ($P < 0.001$) less during the cold phases (2 and 3) and rises slightly above baseline during the rewarming stage.

Figure 4

Figure 4 depicts an index of contractility $[(dp/dt)P^{-1}]$ and again is calculated as a percent of the baseline value. The contractility for all groups is depressed during the cold phases, but it is significantly elevated for phase 3 (6 Hrs-25°C) for the group receiving fluid 2 hours into the cold phase. The contractility for this group does not increase significantly when rewarming is completed, but the other two groups do significantly increase their contractility upon rewarming.

Figure 5

Figure 5 shows the cardiac output (CO) for all three groups for the entire experiment. The initial drop from control to 25°C is greater than 50%. The groups not receiving fluid before rewarming maintain this low cardiac output while the group receiving fluid at 2 Hrs shows a significant increase in CO and some of this increase is maintained over the next four hours.

The final cardiac output for all groups is not significantly different from each other, but it remains depressed when compared to pre-cool levels.

Table 3. Mean calculated total peripheral resistance

Stage	Group 1	Group 2	Group 3
1	131 $\pm$ 8	132 $\pm$ 4	127 $\pm$ 4
2	94 $\pm$ 7	95 $\pm$ 8	82 $\pm$ 9
3	108 $\pm$ 7	101 $\pm$ 6	83 $\pm$ 9
4	139 $\pm$ 11	126 $\pm$ 4	132 $\pm$ 4

Table 3 lists the calculated total peripheral resistance for the three groups using the following formula:

$$\text{TPR (dynes sec/cm}^5\text{)} = \frac{\text{pressure head} \times 13.6 \times 980}{\text{flow (ml/sec)}}$$

The lowered TPR during cold reflects the low arterial pressure and CO during these phases. There is no significant difference in TPR levels after rewarming when compared to pre-cool levels.

DISCUSSION

Figure 1 shows a reduction of about 14% of plasma volume after some time at 25°C. This is in agreement with the work of D'Amato (4) who reported a 12% decrement at 20°C and Lofstrom (10) who reported a 23% decline at 26°C and a 35% drop at 20°C. This decrease in plasma volume is further substantiated by the hemoconcentration as shown in the elevated hematocrit in Figure 2. The big difference is the failure for the hematocrit levels to drop after rewarming and the apparently reestablishment of

the plasma volume. Lofstrom also reported full recovery of plasma volume upon recovery. Figure 2 also shows that normal saline given I.V. during the cold phase will result in an increase in the plasma volume even at some later time (4 Hrs) indicating that at steady state at 25°C, the forces causing water shifting are not as great as they are during changing conditions (cooling or warming).

Kanter (9) has reported no change in plasma Na^+ at body temperatures down to 25°C, but did report a decrease in plasma K^+ . The data presented in Table 1 supports this data with no change in plasma Na^+ and an overall drop in plasma K^+ . This loss of K^+ was explained by Kanter (7) as being due to a shift from plasma to muscle and not due to increased urinary loss. Kanter explained the apparent discrepancy in a decreasing K^+ and a decreasing pH by suggesting greater changes in intracellular pH than in extracellular pH. Data from Table 2 shows that urinary output of K^+ does increase in terms of concentration while the volume is decreasing. Sodium output is less and helps explain the constancy in plasma sodium.

Nonoyama (12) reports that a decrease in pH results in a decrease in cardiac contractile force. The method of the depressed pH was important on the magnitude with metabolic acidosis having a much greater effect and also predisposing the heart to a greater chance of ventricular fibrillation.

Data presented in Figures 3 and 4 shows that as pH decreases, heart rate and cardiac contractility also decrease. What is different is the effect of giving fluid (group 2) on the

contractility. While the pH is no different between the groups at 25°C after 6 Hrs, the contractility of the group having received fluid four hours earlier is much greater (30%). This is reflected in the cardiac output shown in Figure 5, but not in the total peripheral resistance (Table 3).

D'Amato (4) reports that the method of rewarming (fast vs slow) affects the cardiovascular system. Complete return of cardiac output, heart rate cardiac work and blood pressure results when rewarming occurs rapidly (1-1/2 Hrs), but not when slow rewarming (4-1/2 Hrs) occurs. The rate of rewarming for this study was 3°C/Hr or just over 3 hours which is neither fast nor slow. It is clear that some parameters do return to normal or above normal after rewarming, but cardiac output clearly does not. Figure 5 shows the different levels of cardiac output at the start of rewarming, but the level does not affect the end result since no difference exists for the three groups after rewarming.

Berne (2) has reported that hypothermia does not cause a significant impairment of the myocardium. D'Amato (4) reported that 1/3 of his experimental animals suffered cardiovascular collapse during slow rewarming. It appears that some changes are occurring when the animal is cold to change cardiac thresholds or increase cardiac irritability resulting in increased incidence of ventricular fibrillation. D'Amato suggested that the cardiovascular collapse was due to a peripheral vascular phenomenon and not to the heart itself. This conclusion was based on studies involving the infusion of

saline before rewarming and the subsequent increases in cardiac output and minute work.

It is clear from this study and data published by Drake (5), that the addition of normal saline has a minimal long lasting effect and does not really affect the cardiovascular recovery from hypothermia. If normal saline is not effective, than what fluid should be given to hypothermic victims? The usual fluid administered is lactated Ringer solution, but this may be of little use also since it resembles saline and the enzyme systems to utilize lactate are inactivated below 30°C. Another solution that has been used is low molecular weight dextran solution (10%) which has been shown by Drake (5) to increase plasma volume (increased colloid osmotic effect) and to decrease the sludging of the blood.

REFERENCES

1. Barbour, H.G., E.A. McKay, W.P. Griffith. Water shifts in deep hypothermia. AJP 104:9-19, 1944.
2. Berne, R.M. Myocardial function in severe hypothermia. Circ. Res. 2(1):90-95, 1954.
3. Chen, R.Y. and S. Chien. Hemodynamic functions and blood viscosity in surface hypothermia. AJP 235:H136-H143, 1973.
4. D'Amato, H.E., S. Krunheim, B.C. Covino. Cardiovascular functions in the dog rewarmed rapidly and slowly from deep hypothermia. AJP 198(2):333-335, 1960.
5. Drake, C.T., and B.J. Lewis. The plasma volume expanding effect of low molecular weight dextran in the hypothermic dog. Am. Col. Surg., Surg. Forum 12:182-184, 1961.
6. Crossman, W., H. Brooks, and S. Meister. New technique for determining instantaneous myocardial force-velocity relations in the intact heart. Circ. Res. 28:290-297, 1971.
7. Kanter, G.S. Regulation of extracellular potassium in hypothermia. AJP 205(6):1285-1289, 1963.
8. Kanter, C.S. Hypothermic hemoconcentration. AJP 214(4):856-859, 1968.
9. Kanter, C.S. Renal clearance of sodium and potassium in hypothermia. Can. J. of Biochem. and Physiol. 40:113-122, 1962.
10. Lofstrom, B. Changes in blood volume in induced hypothermia. Acta Anaesth. Scandinav. 1:1-13, 1957.
11. Monroe, R.G., R.H. Strang, and C.G. Lafarge. Ventricular performance, pressure-volume relationships, and O₂ consumption during hypothermia. AJP 206(1):67-73, 1964.
12. Nonoyama, A., S. Kotani, and I. Miyamoto. The effect of metabolic and respiratory acidosis on cardiac functions. JPN Circ. J. 34(2):61-67, 1970.
13. Nose, H. Transvascular fluid shift and redistribution of blood in hypothermia. JPN J. Physiol. 32(5):831-842, 1982.
14. Rand, P.W., E. Lacompe, and H.E. Hunt. Viscosity of normal human blood under normothermic and hypothermic conditions. JAP 33(6):117-122, 1964.

DISCLAIMER

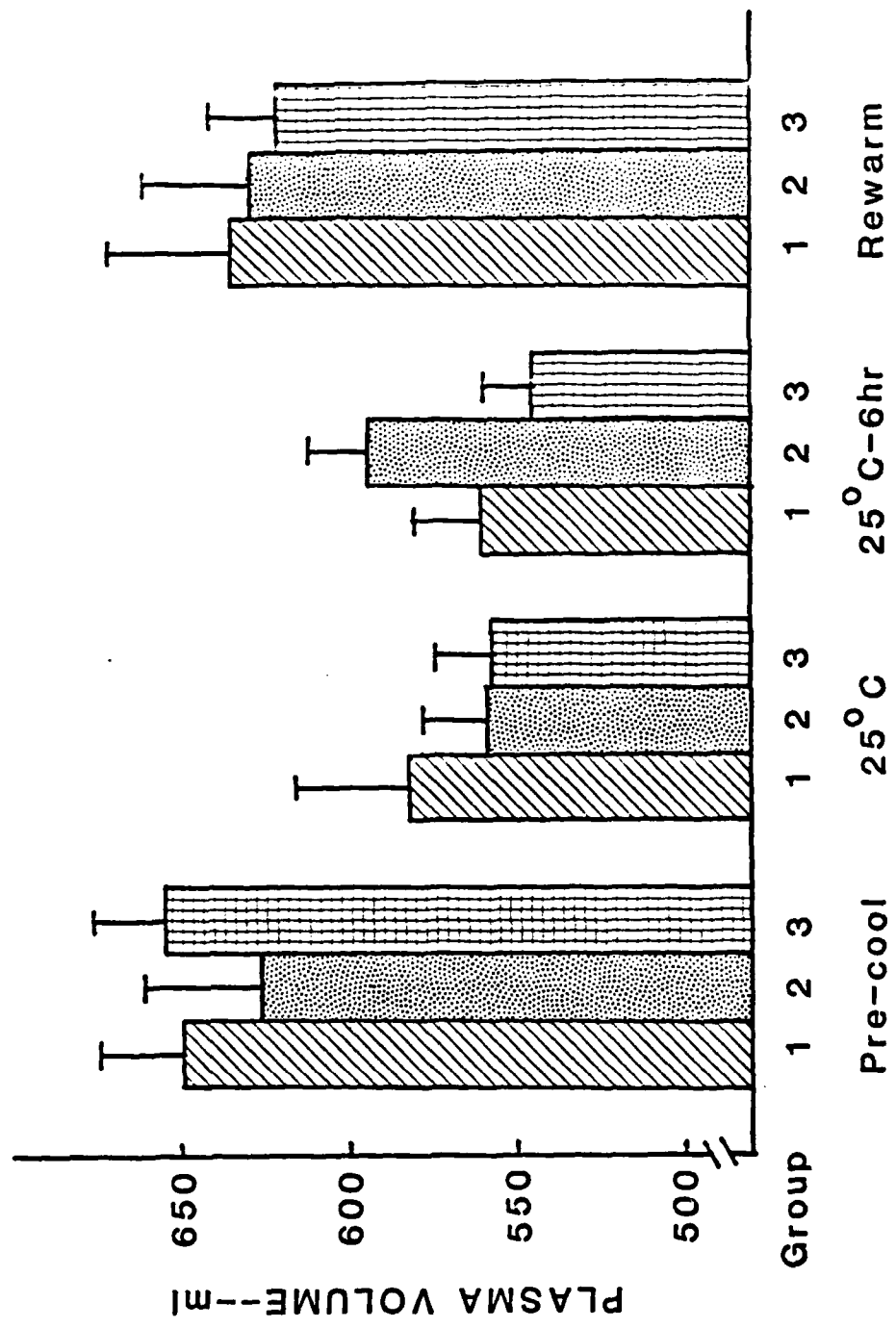
The views, opinions, and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy, or decision, unless so designated by other official documentation.

Human subjects participated in these studies after giving their free and informed voluntary consent. Investigators adhered to AR 70-25 and USAMRDC Regulation 70-25 in Use of Volunteers in Research.

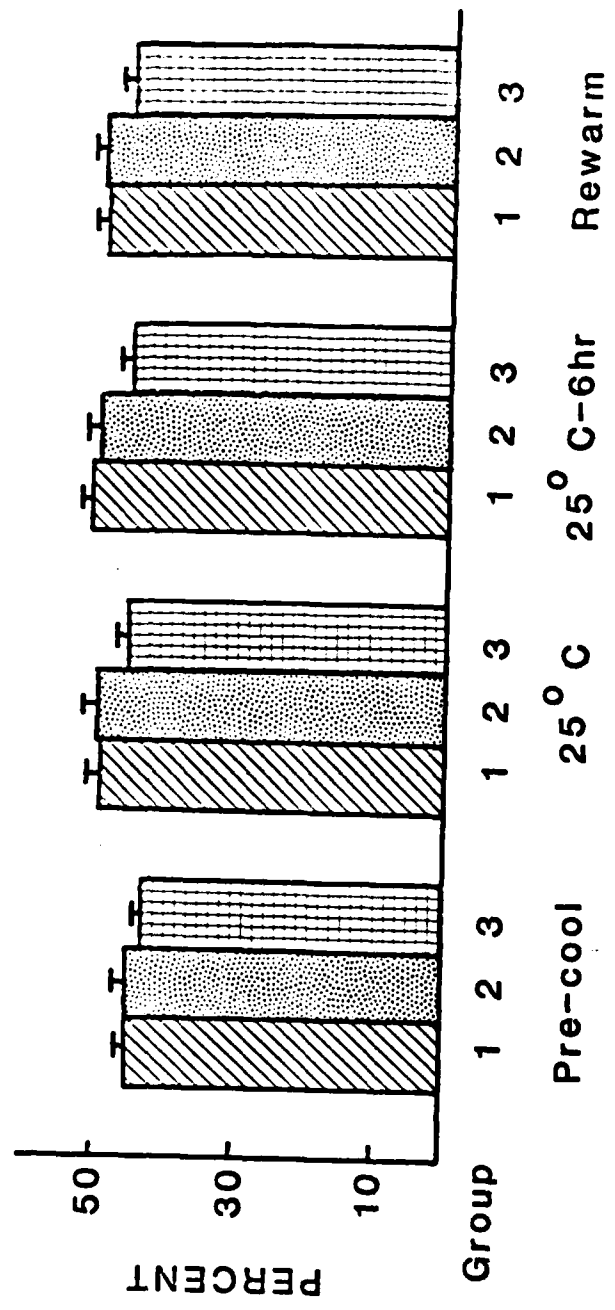
FIGURE LEGENDS

- Fig. 1. Mean plasma volume for three groups across the four study phases.
- Fig. 2. Mean hematocrit percentage for all groups across the study.
- Fig. 3. Mean heartrate as a percentage of baseline levels for all groups.
- Fig. 4. Mean contractility as a percentage of baseline levels for all groups.
- Fig. 5. Mean cardiac output for all groups over the time course of the study.

Fig. 1



25



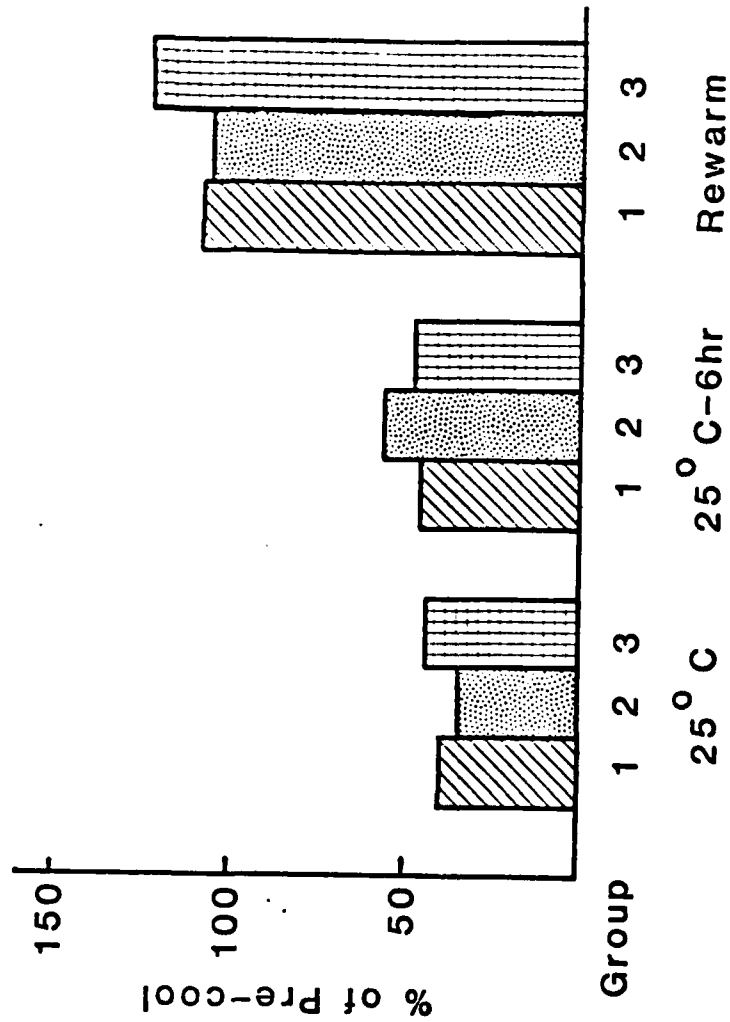
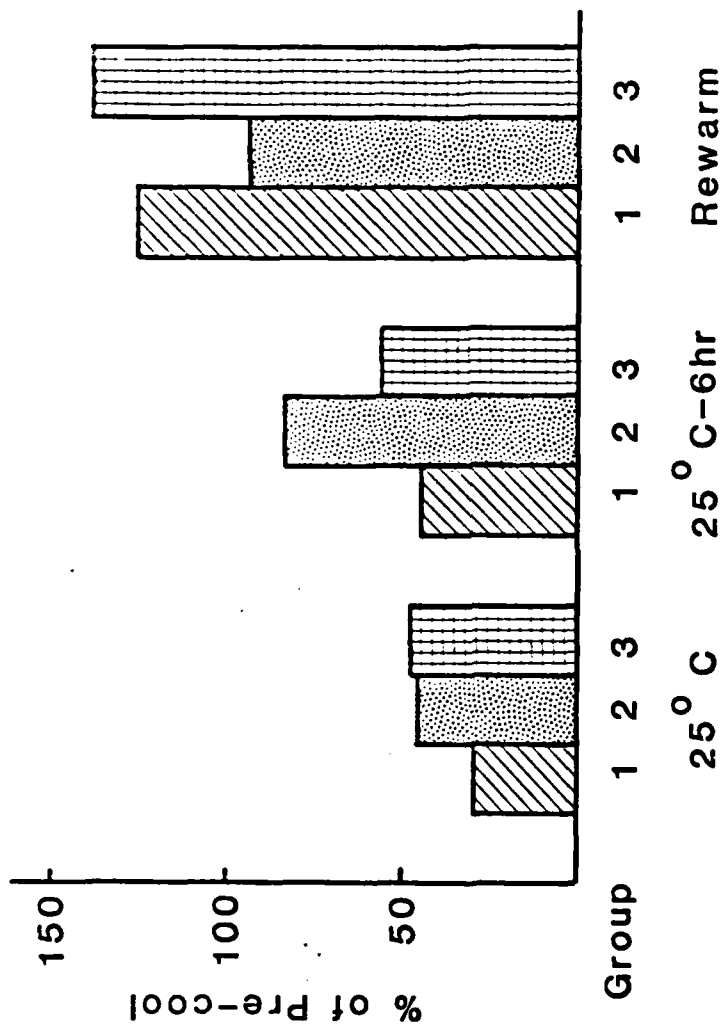
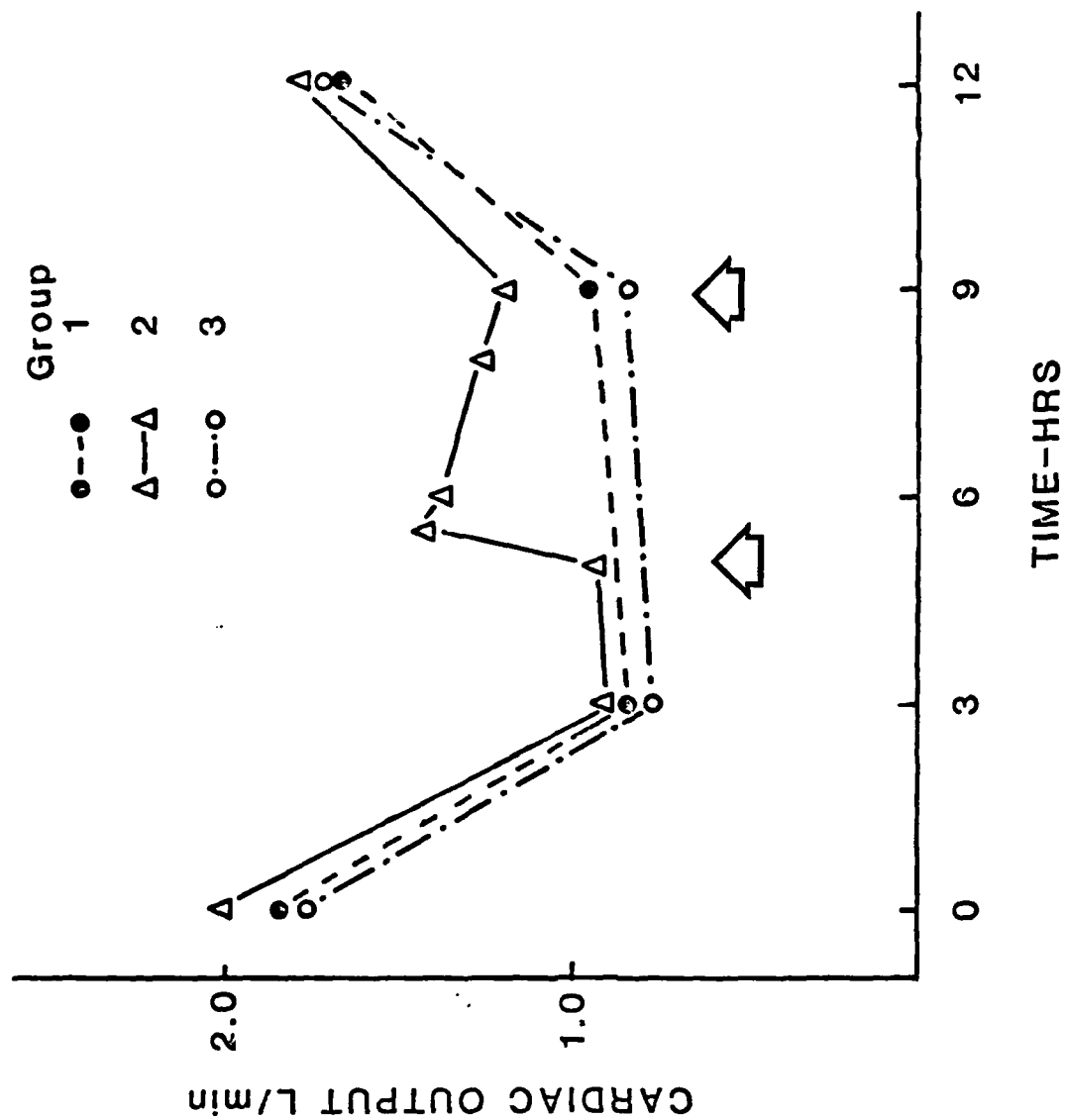


Fig 3
1412

Fig 4





END

FILMED

9-84

DTIC

