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ORAL GLYCEROL SOLUTIONS AS A DETERRENT TO DEHYDRATION DURING HE--ETC(U)
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Heat acclimated rats gavaged with 5% glycerol solutions equivalent to 4% initial body weight excreted less urine during a 3-h heat exposure than did rats gavaged with the same volume of water. C-glycerol studies describe rapid absorption and distribution of glycerol among body tissues.

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ORAL GLYCEROL SOLUTIONS AS A DETERRENT TO DEHYDRATION DURING HEAT EXPOSURE

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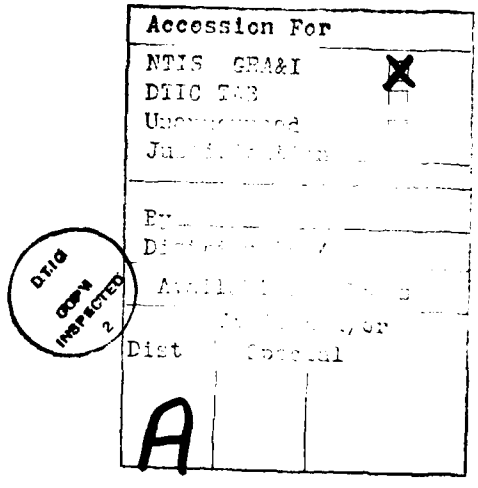
FINAL REPORT

AFOSR-81-0068



The experiments reported herein were conducted according to the principles described in the "Guide for the Care and Use of Laboratory Animals," DHEW Publication No. (NIH) 78-23.

A. Objectives

1. To test the effectiveness of glycerol added to drinking water as a measure for reducing the extent of dehydration during heat exposure.

2. To identify the distribution and metabolism of glycerol administered orally to laboratory rats.

B. Status of the Research

1. Introduction

Dehydration has a detrimental effect on human performance. When dehydration can be expected, i.e., during prolonged periods of work or heat stress or both without adequate fluid replacement, one may reasonably attempt to forestall the onset of significant dehydration by the pre-exposure intake of excess fluids to increase the total body fluids. However, the oral ingestion of common beverages results in rapid renal elimination of excess fluid taken orally and a transitory reduction in both serum electrolyte concentrations and serum osmolarity. If overhydration is to have a significant effect in preventing dehydration, then serum constitutents must not be permitted to decrease; and the addition of an osmotically active substance may be effective in reducing the loss of the excess fluids taken in prior to the heat or work exposure. Glycerol is osmotically active, can be readily administered orally and thereby holds potential as a treatment resulting in overhydration and delaying dehydration.

2. Justification and State of Knowledge in the Field

There are no published reports on the subject of glycerol administration as a treatment for increasing body water although there are reports of clinical situations where the osmotic action of oral glycerol reduces ocular and spinal fluid pressure. As a natural metabolite, glycerol can be administered in large oral doses (1g/kg) every six hours to human subjects. Although the rate of glycerol absorption is rapid, the extent to which a single large oral dose of glycerol will be taken up, metabolized, or stored by various tissues has not been described.

The Thermal Stress Group, Crew Protection Branch, School of Aerospace Medicine (SAM), Brooks Air Force Base (BAFB), have a manuscript currently being reviewed prior to publication (Terrian 1981, personal communication). These investigators observed retention of excess water by resting men following overhydration with a 2% glycerol solution. Their data is best explained by changes in renal function including enhanced water reabsorption by the kidney, a decreased rate of urine production, increased renal reabsorption of water and increased urine to plasma osmolarity ratio. Most of the published glycerol research is concerned with the metabolic pathways and renal excretion of glycerol (see Lin, 1977, for a review).

The distribution of glycerol among body water compartments is apparently dependent upon the rate and dosage of glycerol administration. Following a single pharmacological oral dose the glycerol is distributed throughout 56 to 85% of the body mass (Shafrir and Gorin 1963, Larsen 1963, Holst 1944) whereas continuous intravenous infusion results in glycerol being distributed to only 34% of the body (Wade 1981). Thus the effectiveness of glycerol solutions in producing overhydration can be expected to be dependent upon the timing as well as the dosage.

3. Experiments Conducted

Studies conducted as part of the minigrant (AF09R81-0068) describe a 30 percent reduction in urine production without disturbance of plasma or urine electrolyte concentrations or disturbance of body tissue hydration.

a. Methods & Materials First Series

i. Experimental animals

Male rats (380-440g) were heat acclimated by placing them in individual cages and exposing them to a standard environment (39 C; 21% relative humidity; 20m/min air velocity) five days per week for three weeks.

ii. Experimental Treatments Prior to the Standard 3-h Heat Exposure (10 rats per group)

1. No gavage (tube inserted into and removed from stomach)
2. Water gavage equivalent to 4% initial body weight (IBW)
3. Five percent glycerol gavage equivalent to 4% IBW

iii. Measurements Taken

Urine Volume at 30-min intervals
Feces wt at 30-min intervals
Rectal Temp. - initial and after 2nd & 3rd hour of heat exposure.
Blood samples
  Tail clip after 2-h heat exposure
  Decapitation after 3-h heat exposure
Urine analyses
  Na (flame photometer)
  K (flame photometer)
Blood Analysis
  Hematocrit (duplicate or triplicate)
Serum Analyses
  $[Na^+]$
  $[K^+]$
Body tissues (liver, kidney, heart, skeletal muscle, abdominal fat, stomach, small intestine and skin)
  water content (dried to constant weight at 40 C)

b. Methods & Materials Second Series, ^{14}C-Glycerol Study

i. Experimental animals

Male rats (380-420 g), Heat Acclimated

ii. Experimental treatments

Gavage: 4% IBW, 5% Glycerol with 10 uCi ^{14}C-glycerol

Heat Exposure: 39 C, 21% r.h., 20 m/min Air Velocity

Group 1: 1 h, n = 3
Group 2: 90 min, n = 3
Group 3: 3 h, n = 3

iii. Measurements Taken

^{14}C tissues after 1 h, 90-min or 3 h heat exposure:

liver, kidney, heart, skeletal muscle, abdominal fat, stomach, small intestine and skin.

4. Results, First Series

The 30% reduction in urine volume over a three-hour period (Table I, Fig. 1) is the same reduction in urine volume observed by Terrian et al (Terrian 1981). We have repeated this experiment on several other groups of 10 rats and always had the 30% reduction in urine flow. The urine and serum electrolyte data (Table I, Figs. 2 & 3) indicate there is no major disturbance of electrolyte balance following the glycerol treatment. The hematocrit (Table I, Fig. 4) and tissue water content (Table I, Fig. 5) data also indicate no major disturbance of body water distribution. Drying tissues to constant weight at 40 C is not sensitive enough to indicate the source of the body water lost by the animals not receiving the overhydration (gavage). The extent of rectal temperature elevation was similar for animals receiving no gavage, water gavage or glycerol gavage (Fig. 6). These data along with the saliva evaporated data (Fig. 1) indicate the heat stress was readily tolerated by the animals.

5. Results, Second Series

The data presented in Figure 7 confirms observations reported by other investigators (see Lin 1977 for review). Glycerol is rapidly absorbed. The high counts in liver and kidney indicate catabolism of the glycerol. Because skeletal muscle represents 35% of the body mass a large percentage of the glycerol administered is in the skeletal muscle. The presence of glycerol in muscle, a tissue that does not have enzymes for glycerol catabolism, means that water administered with the glycerol could be stored in the muscle for several hours.

Table I
Data From First Series

Rat		Heat Exposure: No Gavage	Heat Exposure: Gavage 4% Initial Body Weight (IBW) Water	Heat Exposure: Gavage 4% Initial Body Weight (IBW) 5% Glycerol	Prior To Heat Exposure	No Treatment Water ad lib.
Urine Volume, %IBW						
after 3 h	$\bar{X}$	0.6	3.1	2.2		
	SD	0.4	0.7	0.6		
	n	10	10	10		
Saliva Evaporated, %IBW						
after 3 h	$\bar{X}$	4.6	4.2	4.2		
	SD	0.7	0.5	0.6		
	n	10	10	10		
Urine Na, mmole x 10^{-4}/g IBW						
during 1st h	$\bar{X}$	1.6	2.4	2.6		
	SD	0.9	1.1			
	n	9	3	1		
during 2nd h	$\bar{X}$	1.0	1.3	0.7		
	SD	0.4	0.2			
	n	10	3	1		
during 3rd h	$\bar{X}$	0.6	1.4	1.3		
	SD		0.4			
	n	2	2	1		
Urine K, mmole x 10^{-4}/g IBW						
during 1st h	$\bar{X}$	2.7	2.0	3.7		
	SD	1.9	0.8	0.2		
	n	8	4	3		
during 2nd h	$\bar{X}$	2.4	1.6	0.8		
	SD	1.4	1.1	0.7		
	n	11	4	3		
during 3rd h	$\bar{X}$		1.3	0.6		
	SD		0.6	0.2		
	n		3	2		
Serum Na, mmole x 10^{-4}/g IBW						
after 2 h	$\bar{X}$	0.08	0.128	0.14		
	SD	0.003	0.028	0.003		
	n	2	4	3		
after 3 h	$\bar{X}$	0.10	0.13	0.14		
	SD	0.004	0.03	0.02		
	n	2	4	3		
Serum K, mmole x 10^{-4}/g IBW						
after 2 h	$\bar{X}$		0.018	0.015		
	SD		0.001			
	n		2	2		
after 3 h	$\bar{X}$	0.015	0.017	0.017		
	SD	0.001	0.002	0.001		
	n	2	3	2		
Hematocrit						
after 3 h	$\bar{X}$	48.3	52.2	49.0		
	SD	3.3	2.0	2.5		
	n	4	5	8		
T °C, Rectal						
pre heat exposure	$\bar{X}$				37.1	
	SD				0.2	
	n				24	
after 2 h	$\bar{X}$	39.9	39.1	39.1		
	SD	0.5	0.6	0.4		
	n	10	10	10		
after 3 h	$\bar{X}$	40.1	39.9	39.7		
	SD	0.4	0.1	0.3		
	n	4	6	9		
Tissue, % Water Content		(n=5)	(n=7)	(n=8)		(n=3)
liver	$\bar{X}$	67.8	67.7	67.0		67.2
	SD	0.7	1.1	1.1		0.3
kidney	$\bar{X}$	74.2	73.3	73.0		75.2
	SD	0.9	1.7	2.4		0.2
heart	$\bar{X}$	75.0	76.0	75.5		75.3
	SD	0.9	0.8	0.6		0.4
skeletal muscle	$\bar{X}$	74.0	74.2	74.6		73.5
	SD	0.4	0.5	0.5		0.2
skin	$\bar{X}$	47.2	46.1	50.2		48.2
	SD	3.3	4.9	4.4		1.2
abdominal fat	$\bar{X}$	6.2	6.2	7.8		6.2
	SD	1.9	2.0	2.1		0.4

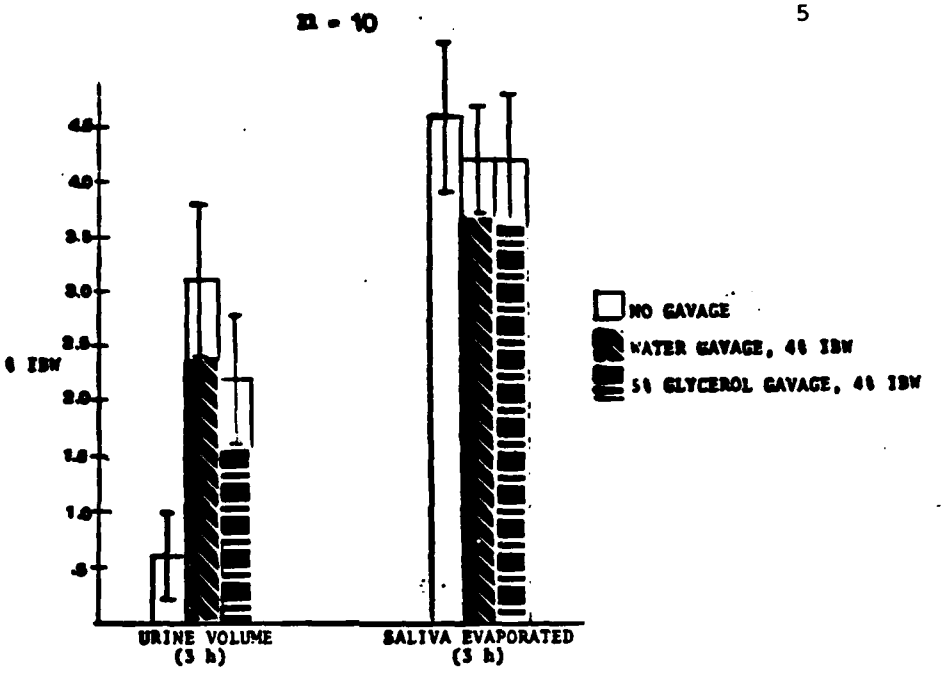


Figure 1. Urine excreted and saliva evaporated expressed as percent of initial body weight (IBW) during 3-h heat exposure of control and gavaged heat-acclimated rats. n = 10.

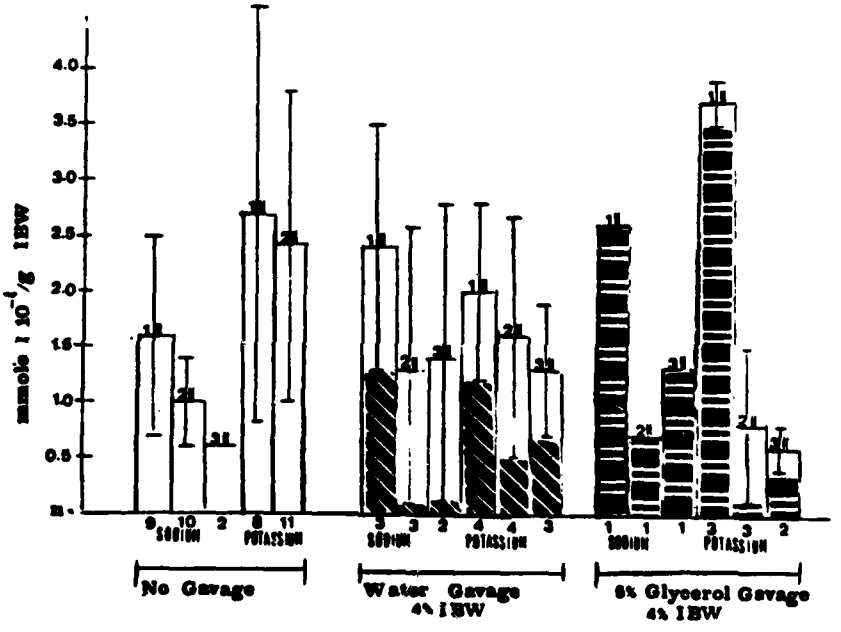


Figure 2. Urine sodium and potassium concentrations (mmole x 10^{-4}/g initial body weight) at hourly intervals by control and gavaged rats after 3-h exposure.

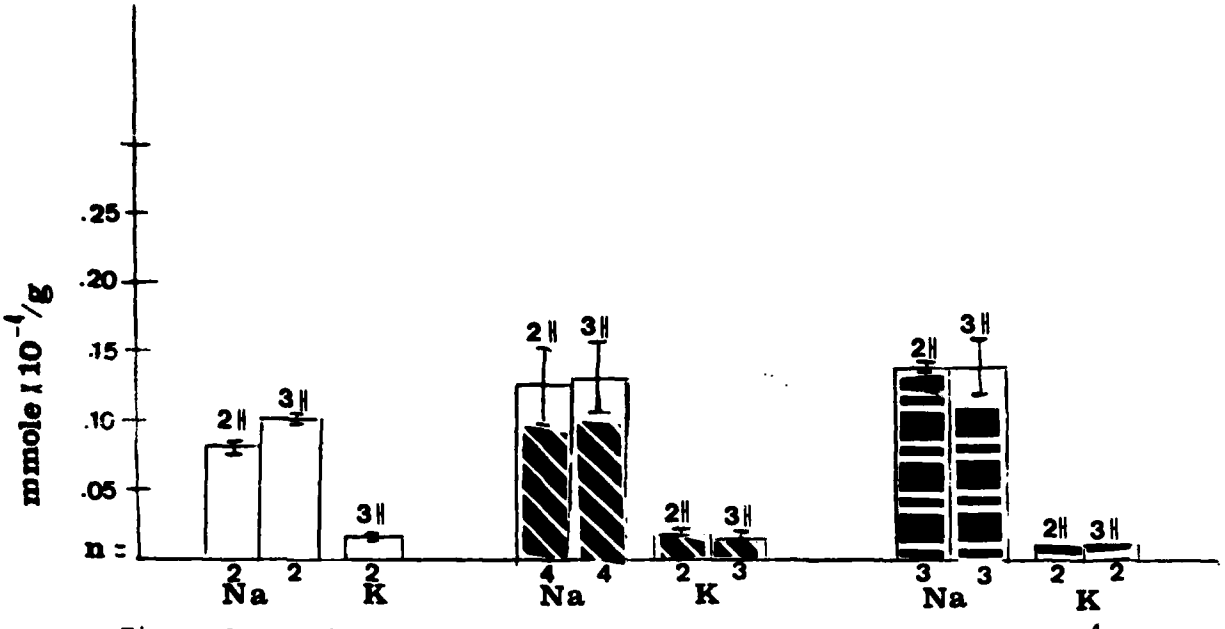


Figure 3. Serium sodium and potassium concentrations (mmole x 10^{-4}/g) after 2- or 2-h exposure.

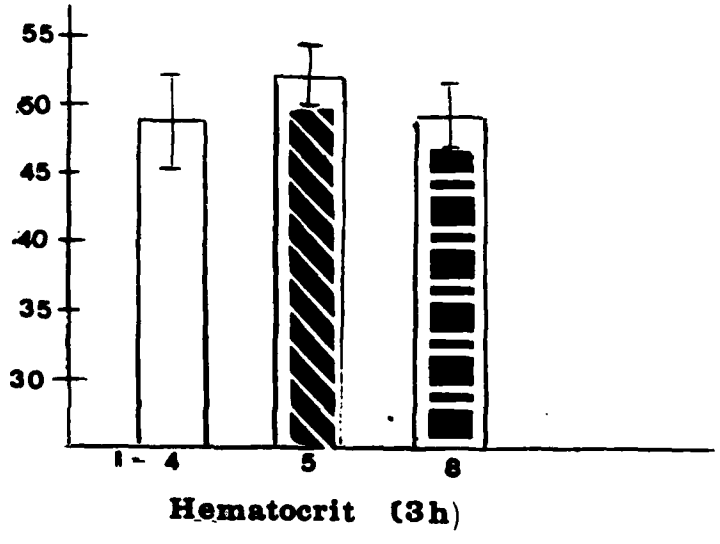


Figure 4. Hematocrit after 3-h heat exposure.

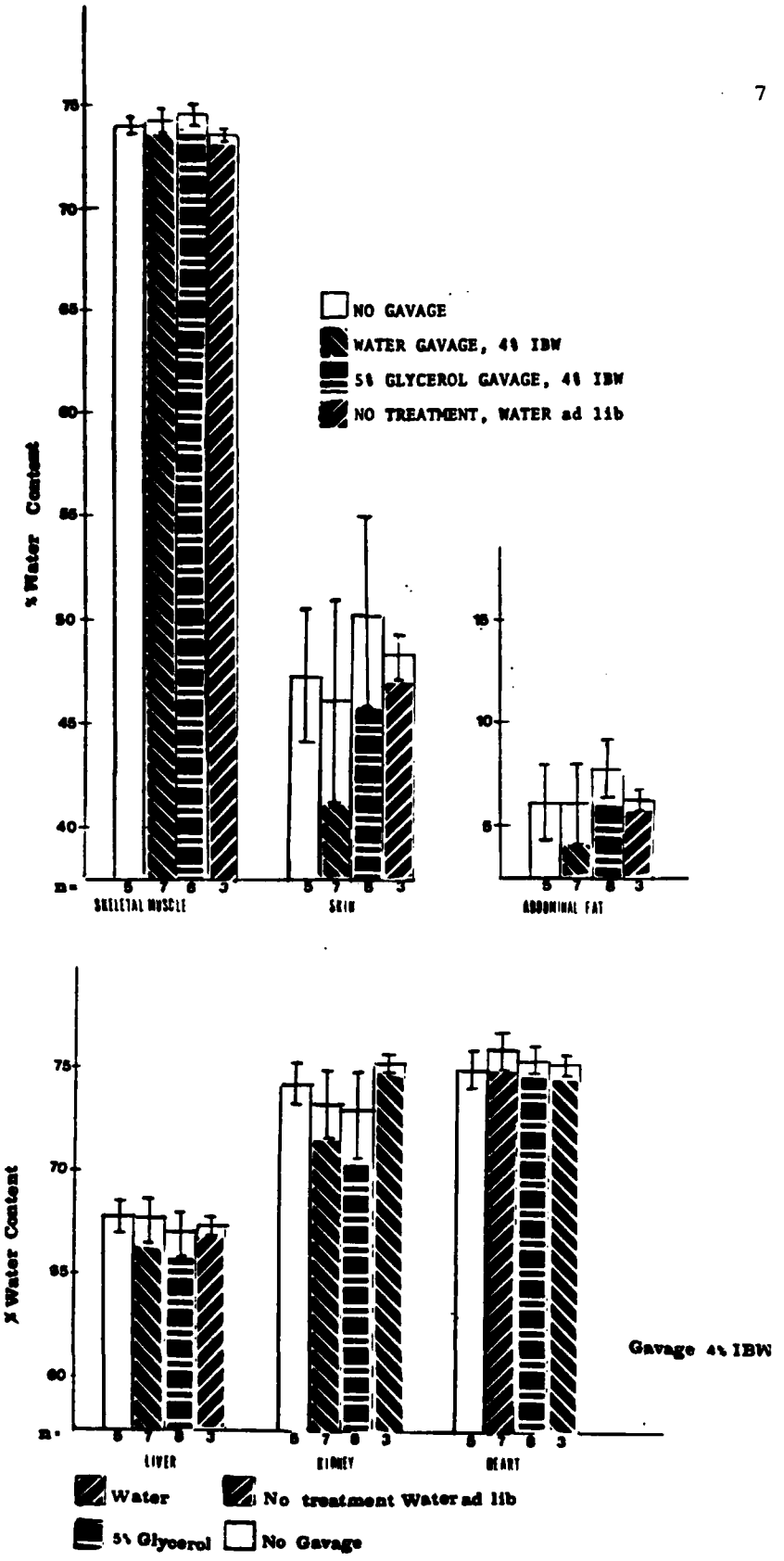


Figure 5. Percent water content of tissues after 3-h heat exposure. Three experimental groups had no water available during the heat exposure. The fourth, no treatment, group had water ad lib throughout the experiment.

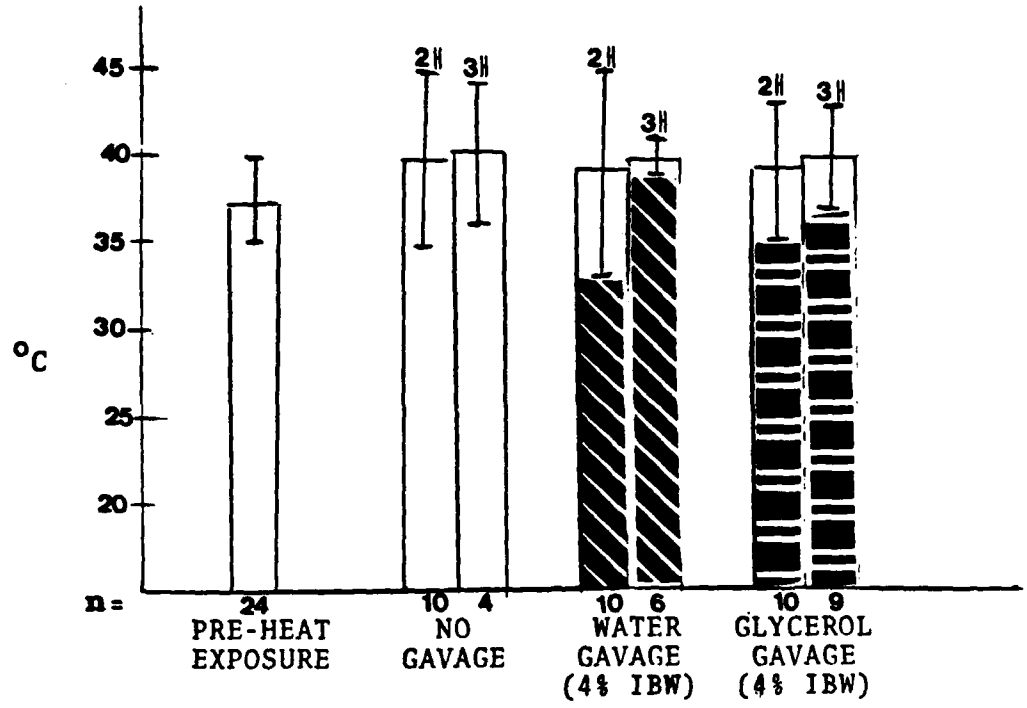


Figure 6, Rectal temperature, °C, prior to and after 2- or 3-h heat exposure.

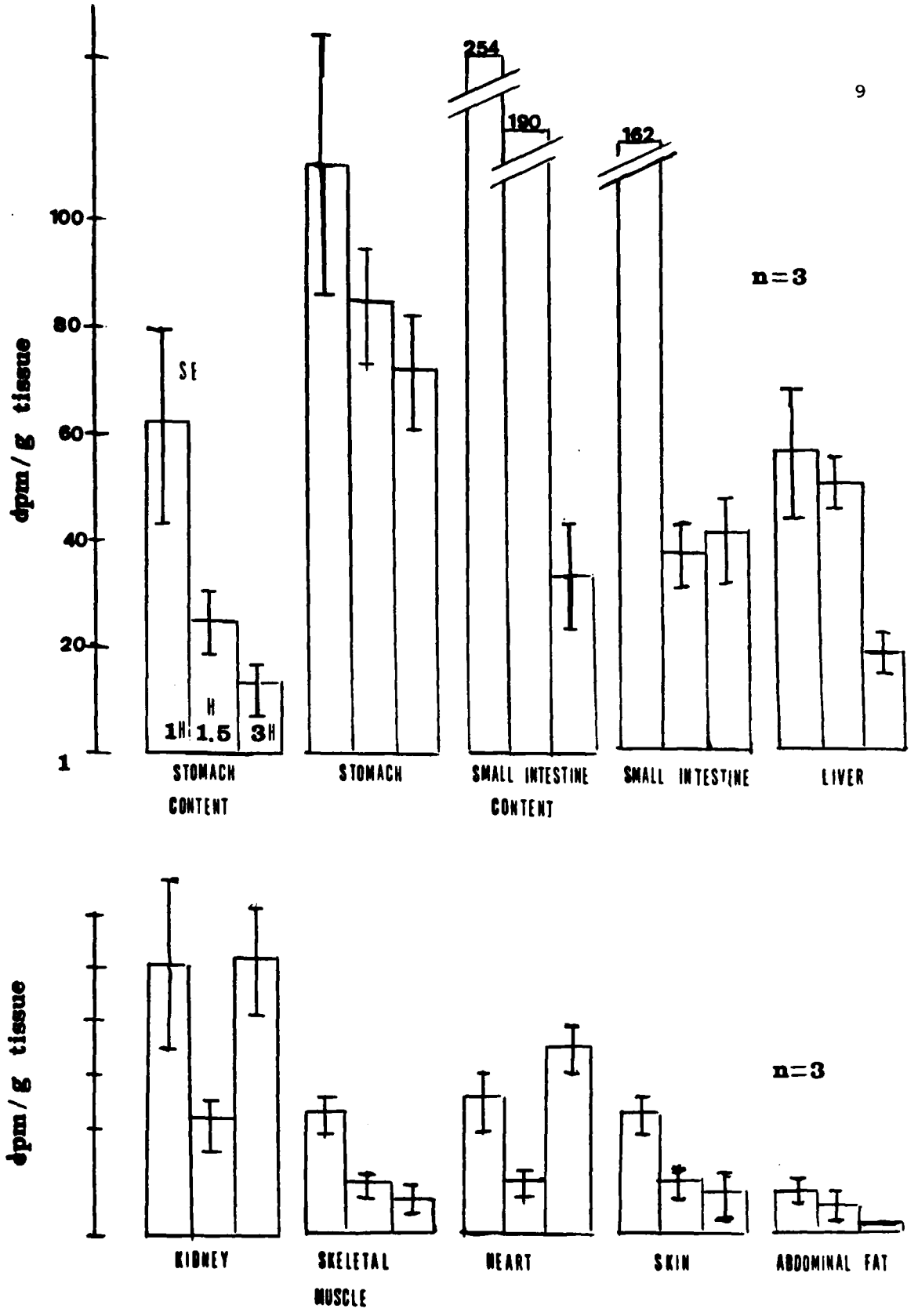


Figure 7. Distribution of ^{14}C, dpm/g, among body tissues. Rats were placed in the hot environment immediately after injecting ^{14}C-glycerol. Three rats were sacrifieced after 60, 90 and 180 min heat exposure.

6. Discussion of First and Second Series

Glycerol is readily distributed among body tissues. The question of potential for glycerol solutions to produce overhydration of body tissues remains open. The curious point of a decrease in urine volume in the heat exposed glycerol treated animals serves as the best clue we have of glycerol solutions having a potential for producing overhydration. Among our pilot studies, non-heat acclimated rats given the same glycerol solutions did not always have the reduced urine volume. The difference in the response to glycerol solutions by heat acclimated and nonacclimated rats may be related to the expanded blood volume of the heat acclimated rats. The expansion of blood volume following heat acclimation in men has been attributed to increased serum protein (Senay 1979). Posture and type of exercise has also been reported to be responsible for shifts in plasma proteins (Harrison et al 1981). A systematic long-term study of various glycerol solutions administered at various time intervals is needed to describe the potential overhydration possible by administering glycerol solutions.

7. Significance

Oral administration of 5% glycerol equivalent to 4% initial body weight can reduce the volume of urine produced during a 3-h heat exposure by heat acclimated rats.

8. References Cited

Harrison, M.H., R.J. Edwards, M.F. Graveney, L.A. Cochrane and J.A. Davies. 1981. Blood volume and plasma protein responses to heat acclimitization in humans. J. Appl. Physiol. 50:597-604.

Holst, E.J. 1944. Glycerol oxidation in the animal organism Acta Physiol. Scand. 7:69-79.

Larsen, Jens Anker. 1963. Elimination of glycerol as a measure of the hepatic blood flow in the cat. Acta Physiol. Scand. 57:224-234.

Lin, E.C.C. 1977. Glycerol utilization and its regulation in mammals. Ann. Rev. Biochem. 46:765-795.

Senay, L.C. Jr. 1979. Effects of exercise in the heat on body fluid distribution. Med. Sci. Sports 11:42-48.

Shafrir, E., and E. Gorin. 1963. Release of glycerol in conditions of fat mobilization and deposition. Metab. Clin. Exp. 12:580-587.

Terrian, D.M. 1981. Personal communication of a manuscript in preparation for publication entitled, Oral Glycerol Prolongs Retention of Excess Water in Man by David M. Terrian, Donald M. Tucker, Sarah A. Nunneley, and Loren G. Myhre, USAFSAM/VNB, Brooks AFB.

C. Publications resulting from research

None to date

D. Professional Personnel Associated with the Research

Jane E. Agnew & Mark P. Hogan, undergraduate seriors, received credit in Biology 499, Special Problems, for their participation in this research.

E. Interactions

Overhydration of laboratory rat with glycerol solutions. Jane E. Agnew and M.L. Riedesel. 1981. Paper presented at the fall meeting New Mexico Academy of Science

F. Patent Disclosures and Specific Application

None

G. Other comments

None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