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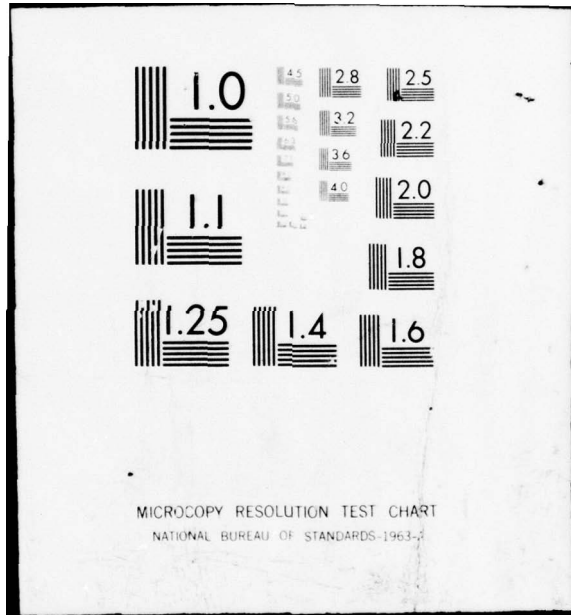
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THE EFFECTS OF ABRUPT ALTITUDE EXPOSURE (4300 M) UPON THE METABOLISM OF GLUCOSE-¹⁴C-UL IN MAN

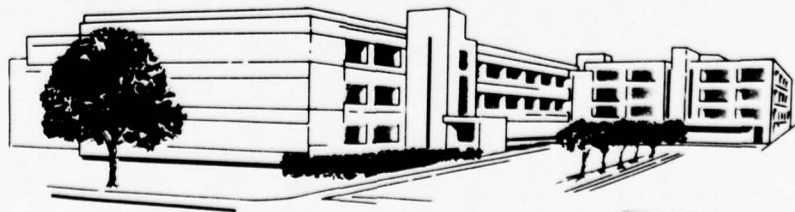
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glycogen stores in the 40-hour exposed men. Plasma levels of growth hormone were increased 6-10 fold during the first four hours at 4,300 meters. Insulin levels were increased after glucagon infusion in both altitude-exposed men and control men concomitant with increased plasma glucose values although the increases were not significantly correlated. These data indicate that glucose catabolism was enhanced during initial altitude exposure with an increased requirement for carbohydrates.

ABSTRACT

The catabolism of infused ^{14}C -glucose in sea-level natives was compared during initial altitude exposure and at sea level. An increased disappearance of plasma radioactive glucose in two studies and an increased production of $^{14}\text{CO}_2$ in the second study were observed. Fasting plasma glucose levels decreased with increased duration of altitude exposure. Altitude exposure enhanced glucagon-mediated hyperglycemia. A shorter duration of hyperglycemia and reduced glucose levels after glucagon suggest a depletion of liver glycogen stores in the 40-hour exposed men. Plasma levels of growth hormone were increased 6- to 10-fold during the first four hours at 4,300 meters. Insulin levels were increased after glucagon infusion in both altitude-exposed and control men concomitant with increased plasma glucose values although the increases showed no significant correlation. These data indicate that glucose catabolism was enhanced during initial altitude exposure with an increased requirement for carbohydrates.

PREFACE

Co-authors C. Frank Consolazio, deceased December 1976, was with Letterman Army Institute of Research as Chief of Bioenergetics Division until the end of his career; Raymond F. Burk, M.D., is now affiliated with the Liver-GI Unit, University of Texas Southwest Medical School, Dallas, Texas 75234; Ted A. Daws is affiliated with the staff of Fitzsimons General Hospital, Denver, Colorado, and Edward G. Lufkin, M.D. is now affiliated with the Department of Endocrinology and Internal Medicine, Mayo Clinic, Rochester, Minnesota 55901.

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INTRODUCTION

Abrupt exposure of men to altitude of 4,000 meters or more usually produces a clinical syndrome which includes headaches, anorexia, nausea, vertigo, and sometimes vomiting. Maintaining adequate intakes of carbohydrates either with high carbohydrate diets (1) or with normal intakes of a balanced diet (2) reduced these symptoms. Mitchell and Edman (3) reviewed the literature on effects of diet upon tolerance to hypoxia and concluded that high carbohydrate diets were slightly beneficial, high fat diets produced questionable effects, and high protein diets were detrimental for a period of 1 to 8 hours post prandially. Forbes (4) reported that fasting blood sugar levels decreased as men went from sea level to 3,600 m, and then increased at higher elevations. More recent studies (5-7) indicate that altitude natives had reduced levels of fasting blood sugar which are possibly attributable to their different food habits. During the 44-day exposure of 5 American athletes to 3,992 m (7), plasma glucose levels were unchanged, however, red blood cell content of glucose was reduced 14-30% thereby the whole blood glucose levels were reduced. Glucose tolerance tests were performed at 5,340 m by Forbes (4), who reported that after ingestion of 100 g glucose, two subjects showed increases of only 6 and 2 mg/100 ml after 17 days, while the third subject showed a 38 mg/100 ml increase in blood sugar level after only 6 days of exposure. Substituting sucrose for the glucose and repeating the test in the first two subjects produced the same results, i.e., a 4 mg/100 ml rise. One week after return to sea level, the first 2 subjects had normal blood sugar tolerances with elevations of 38 and 52 mg/100 ml, while the third man had abnormal glucose tolerance. Forbes (4) suggested that the altered glucose tolerances at altitude may have been related to semi-starvation.

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1. Consolazio, C.F. et al. Fed Proc 28:937, 1969
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 3. Mitchell, H.H., and M. Edman. Nutrition and resistance to climatic stress with particular reference to man. Research Report. USA QM Institute, 1949
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 5. Picon-Reategui, E. Metabl Clin Exptl 11:1148, 1962
 6. Picon-Reategui, E. Fed Proc 25:1233, 1962
 7. Picon-Reategui, E. et al. J Appl Physiol 29:560, 1970

Picon-Reategui (5, 6) conducted both oral and intravenous glucose tolerance tests on high-altitude natives and sea-level inhabitants at their respective altitudes of residence. The normal Peruvian diet consumed by these men contained 14% or less fat, 70% or more carbohydrate, and 8% protein for the altitude subjects, and 16% protein calories for the sea-level group. In both studies, glucose utilization appeared to be higher in the altitude group than for the sea-level subjects. Janoski et al. (8) administered glucose tolerance tests to sea-level men before and within 5 days after abrupt exposure to 4,300 m during two separate studies. In the first study, food consumption averaged only 900 kcal/day during the altitude phase, and the plasma glucose levels were greatly elevated after oral glucose load as compared to the same tests at sea level. Food consumption was maintained at about 3,400 kcal/day in the second study, and glucose tolerances were similar to those at sea level. This indicated that a glucose intolerance developed at altitude only in men who restricted their intakes of food.

Although some reports (3, 9) have suggested that carbohydrate was the preferred nutrient at altitude, especially after abrupt exposure, no controlled studies have objectively evaluated varying nutrient intakes until recently (1, 2). All-liquid diets of either normal or high carbohydrate contents were fed for 27 days, which probably resulted in dietary monotony enhancing the anorexia during altitude exposure. Clinical symptoms were reduced and work performance was increased in the high-carbohydrate-fed group when compared with the group receiving the normal diet. Food consumption was maintained in a second study by providing half of the intake as normal foods for 18 days; however, the dietary differences disappeared. The lack of dietary effect in the second study was attributed to the high carbohydrate intake (418g/man/day) of the normal diet group compared to only 320 and 237g of daily carbohydrate intakes for the high and normal carbohydrate-fed men of the first study. This would appear to indicate a daily requirement of about 300g carbohydrate to minimize symptoms after abrupt altitude exposure. To obtain further information on carbohydrate metabolism in men abruptly exposed to altitude, these studies were conducted by infusing labeled glucose.

SUBJECTS AND METHODS

Two similar studies were conducted during successive summers. The participants were healthy male volunteers 18 to 24 years old, who had lived within 500 m of sea level for their entire lives. The subjects were matched in pairs as to height, weight, and age. One man from each pair was abruptly exposed to 4,300 m altitude, while the second served as a sea-level control. Liquid diets of 3,000 kcal (Table 1) containing

8. Janoski, A.H. et al. Fed Proc 28:593, 1969

9. Van Liere, E.J. Arch Intern Med 113:418, 1964

13.7, 40.0, and 46.3% calories of protein, fat, and carbohydrate, respectively, were divided into 4 meals/day and fed for 3 days prior to altitude exposure. The sea-level control subjects received the amounts of diet consumed by their altitude mates on a pair-feeding schedule two weeks later. During the sea level studies, the subjects lived and were studied in an air conditioned barracks in Texas (less than 300 m altitude). The altitude group lived and was studied in a combined laboratory and living quarters heated so that the temperature differential between the two sites was minimal. In both studies, travel from sea level to altitude was accomplished in 4 hours by air, and 2 hours by surface (in the second study, the 3.5-hour delay was at 1,600 m between the air and surface travel). The altitude and sea-level subjects were studied in the morning after at least 12 hours of fasting except for the immediate exposure group and their controls of the second study who were studied between 1300 and 1800 hours after at least 6 hours of fasting.

In the first (pilot) study, six men were infused with 30 μCi of ^{14}C -glucose (specific activity of 180 Ci/mole) after 16-18 hours of altitude exposure; the remaining six men after 40-42 hours at 4,300 m. Blood samples for glucose and ^{14}C -glucose determinations were obtained before infusion and at 15, 25, 40, 55, and 65 minutes post infusion. At this time, 70 μg of glucagon were rapidly infused and blood samples were taken at 1, 5, 10, 15, 20, and 30 minutes for the determination of plasma specific activities (10). Expired $^{14}\text{CO}_2$ was monitored continuously from 10 minutes before injection until 20 minutes after injection of radioactive glucose, and then 3-1/2 hours after injection it was monitored for 30 minutes.

The design of the second study was for 3 volunteers to be translocated to altitude and 3-1/2 hours later, 3 more volunteers were translocated. In each group of 3 volunteers one man received the glucose within 2 hours, one after 16 hours and the third after 40 hours of altitude exposure. Four days later, 6 more men were to be transported to altitude and infused on the same schedule. Since two of the altitude volunteers were unable to participate, the design was changed and 3 men were studied immediately: 4 after 16 hours and 3 after 40 hours at altitude. After a control blood sample was obtained, 30 μCi of ^{14}C -glucose was infused intravenously and blood samples were taken at 15, 30, 60, 90, and 120 minutes. At this time, 70 μg of glucagon were infused intravenously and blood samples were obtained at 5, 10, 15, 20, 30, 40, and 50 minutes. Continuous monitoring of O_2 consumption and CO_2 production was accomplished with the continuous respiratory gas analyzer (11) and $^{14}\text{CO}_2$ was measured with the electrometer which had a 4.3 liter chamber (12).

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10. Sanbar, S.S. Metabolism 16:259, 1967
 11. Nelson, R.A. et al. Report No. 318. USAMRNL, May 1968
 12. Tolbert, B.M. Ionization chamber assay of radioactive gases. UC Radiation Laboratory Report No. 3499. Department of Commerce, 1956

Whole blood and plasma glucose values were determined by the automated glucose oxidase method (13). After separation of glucose by column chromatography (10), glucose in the elute was measured with o-toluidine (14) and ^{14}C with a Beta spectrophotometer. Plasma insulin was determined by the methods of Makulu et al. (15) and Herbert et al. (16); growth hormone was measured by the use of techniques developed by Schalach and Parker (17).

Nude fasting body weights were obtained to the nearest 20g every morning, immediately after the subjects arose and voided. All statistical analyses were done by either the random or paired-t test with significance tested at the 5% level of confidence.

RESULTS

The average body weights of the subjects are summarized in Table 2. When exposed to altitude, significant weight losses were observed for both studies, while the pair-fed controls did not have significant losses. Weight losses were greater in the first study (1.21 kg/man) as compared to the second study (0.70 kg/man) for two days of altitude exposure. Reduced caloric intakes (Table 3 - 52% for day 1 and 18% for day 2 of altitude exposure) contributed to the weight losses in the first study as compared with only a 10 to 15% reduction of intakes noted during the second study.

Plasma glucoses (Fig. 1) were reduced in the altitude-exposed men in both studies; however, the reductions were significant for only the 40-hour exposed groups. Since no significant differences existed among the altitude-exposed groups in either study, statistical evaluation for the combined data showed that all the altitude values for plasma glucose (except after glucagon) were significantly reduced in comparison to control values. In the first study, the glucagon-induced hyperglycemia at 30 minutes after infusion was less in the 16-hour altitude-exposed men than in sea-level controls. In the second study, the glucagon-induced hyperglycemia was reduced in comparison to controls from 30 through 50 minutes after infusion. The initial glucagon response was faster in all of the altitude-exposed men in both studies.

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13. Tammes, A.R., and C.D. Nordschow. *Am J Clin Pathol* 49:613, 1968
 14. Moorehead, W.R., and E.A. Sasse. *Clin Chem* 16:285, 1970
 15. Makulu, D.R. et al. *Diabetes* 18:660, 1969
 16. Herbert, V. et al. *J Clin Endocrinol* 25:1375, 1965
 17. Schalach, D.S., and M.L. Parker. *Nature* 203:1141, 1964

The specific activities of plasma glucose after infusion of ^{14}C -glucose are depicted in Figure 2. Neither altitude exposure nor length of time at altitude had any effects upon the specific activities of plasma glucose. The 16-hour exposed group in the first study showed an immediate and drastic reduction of specific activities after glucagon. In Study One, both the 40-hour altitude-exposed men and their controls had a slight increase of counts/mg of glucose at one minute after glucagon administration. The largest decrease in specific activities observed in the second study was in men infused immediately after altitude exposure.

The levels of radioactivity that remained in the plasma at various times after infusion are summarized in Figure 3. The disappearance rates of ^{14}C -glucose were similar in all groups with no apparent effects of altitude exposure or duration of time at altitude before infusion. The increased activities of the 40-hour altitude-exposed group and their controls immediately after glucagon infusion were again observed.

The specific activity of expired CO_2 was calculated (for the second study) from continuous measurements of expired CO_2 and $^{14}\text{CO}_2$ (Fig. 4). The increased specific activity that was observed for the "0-hour exposed group" at one hour after infusion of ^{14}C -glucose was not significant, while the elevation for the 40-hour exposed group was significant from 20 to 60 minutes after infusion. The quantities of radioactivity expired per minute are plotted in Figure 5. Although the altitude subjects expired more $^{14}\text{CO}_2/\text{min}$ than the sea-level controls at most time periods, significance was noted for the individual groups only at 195 and 205 minutes for the "0-hour exposed group"; 105 minutes for the 16-hours-at-altitude group, and 125 and 165 minutes for the 40-hours-at-altitude group. There were no significant differences between the altitude groups or control groups; therefore, the data were combined and the altitude-exposed men excreted significantly more $^{14}\text{CO}_2$ than the controls for the period between 60 and 140 minutes after infusing the labeled glucose.

Total $^{14}\text{CO}_2$ expired after infusion of radioactive glucose was calculated (Fig. 6). These excretions were essentially the same in all groups for the first hour. Although the altitude-exposed subjects expired 13 to 27% more $^{14}\text{CO}_2$ than their respective controls for the following 2 hours, no significance could be obtained for these differences until all of the altitude subjects were combined into one group for comparison with the combined control group. The 17% increase of the combined altitude group's excretions were significant from 130 to 190 minutes after infusion.

A summary of plasma insulin values is presented in Table 4, and human growth hormone in Table 5. The insulin values were so variable between subjects and times for each subject that only occasional elevations were significant. The combined data for all of the altitude subjects

would indicate that the insulin elevation after glucagon was more prolonged at altitude than at sea level; however, these differences are essentially the same as those observed at sea-level control days 1 and 2. The human growth hormone data also were erratic. The altitude groups generally had significantly higher plasma values before altitude exposure than the sea level men. Although it was not significant because one of the 3 men did not show the response, two men who were studied immediately after altitude exposure had extremely high growth hormone levels.

DISCUSSION

Anorexia was again observed during altitude exposure, especially in the first study where the intakes by the volunteers were 50% less on the first full day at altitude than at sea level. However, these consumptions were increased on the second day at altitude. During the second study, food consumption was less affected by the altitude exposure with intakes only 10 to 15% less than the preceding days. The weight changes reflect the decrease in intakes with weight losses of 1.21 kg (study one) and 0.70 kg (study two) in the altitude-exposed subjects. The pair-fed sea-level control subjects had minimal weight losses of 0.44 kg in the first study and none in the second study. This indicated that about 0.7 to 0.8 kg of the weight loss observed at altitude probably was due to hypohydration. This agrees with the results of our earlier studies (18, 19), which showed water losses of 2.08 to 2.37 kg for 10 days and 0.52 kg for 6 days at altitude. Hypohydration appears to be partially attributable to hypoxia since it occurs with minimal caloric restriction, and, therefore, does not appear to be due to decreases in caloric intakes.

Reduced plasma glucose levels have been previously reported in both high altitude natives (5-7) and lowlanders during altitude exposure (4). However, the only study on the effects of glucagon upon plasma glucose levels at altitude was done on altitude residents (20). Although the response to the glucagon infusion appeared to be more rapid at altitude than at sea level (indicating a greater sensitivity to glucagon during hypoxia), these differences were not significant. In the first study, plasma glucose levels decreased faster in the 16-hour altitude-exposed men than their sea-level controls, which could indicate a depletion of liver glycogen stores, since the men had fasted about 10 hours before the testing. This shortened duration of glucagon effects was not observed in the second study.

The 40-hour exposed group in the second study also had a shorter

18. Consolazio, C.F. et al. *Am J Clin Nutr* 25:23, 1972

19. Johnson, H.L. et al. *Fed Proc* 28:1195, 1969

20. Picon-Reategui. *Fed Proc* 25:1233, 1966

duration of the glucagon-induced plasma glucose elevation, which could be due to either an increased rate of glucagon destruction or the depletion of liver glycogen stores. Since the post-glucagon glucose levels were lower than the pre-glucagon levels, it would appear that glycogen stores were depleted. Reduced glycogen stores during altitude exposure may be the reason that glucose tolerance tests did not produce as large an elevation in blood glucose levels at altitude as at sea level (4-6). Reduced glycogen stores could enhance glycogen synthesis thereby removing the excess glucose from the plasma. Picon-Reategui (20) reported a reduced hyperglycemia after the infusion of 1 mg of glucagon in high altitude natives as compared to the effect in sea level men. The differences between his results and ours may be attributable to the differences between high altitude natives and sea level natives abruptly exposed to altitude. The men in our studies were probably under greater stress since they were adjusting to this environment, while Picon-Reategui's subjects had lived their entire lives under hypoxic conditions.

The specific activity of plasma glucose was essentially the same in the altitude and control groups throughout the monitoring periods. The decreases in specific activity after glucagon is, of course, due to the dilution of tracer by glucose derived from liver glycogen stores. It appears that some of the labeled glucose was incorporated into glycogen stores during the first hour in the first study, and during the first 2 hours after infusion of the tracer in the second study because there was a slight increase in specific activity (especially per ml of plasma - Fig. 3) after administration of glucagon. This increased radioactivity in the plasma appears concomitantly with the elevation of plasma glucose. Since glucagon increases plasma glucose by stimulating glycogenolysis in the liver (21), the increased radioactive glucose would appear to be released from liver glycogen.

During the first 10 minutes after glucose infusion (represented by the 5 minute points in Figures 4 and 5) little $^{14}\text{CO}_2$ was expired since the tracer had to be transported intracellularly and then catabolized before any $^{14}\text{CO}_2$ would be released for expiration. Appearance of radioactivity was as rapid at altitude as at sea level, which suggests that glucose transport into cells and metabolism were not adversely affected by altitude. In fact, the specific activity of expired CO_2 was significantly higher between 20 and 60 minutes after glucose infusion in the 40-hour altitude group, while their plasma specific activities were lower in comparison to sea-level control men. Therefore, a greater amount of the infused glucose must have been catabolized by the altitude-exposed men than by the control subjects. The uptake of this glucose by cells may have occurred rapidly, which would explain the reduced activity in the plasma at 15 minutes. The respiratory quotient was not increased during this period although it was increased from 80 through 220 minutes

21. Sutherland, E.W. et al. Fed Proc 14:289, 1955

(end of monitoring period), which is consistent with the hypothesis that glycogen stores by glycogenolysis could have resulted from an enhanced utilization of carbohydrate as an energy source.

Enhanced glucose metabolism at altitude was shown by the increased amount of labeled carbon that appeared in the respired gases both on a per-minute and total-time basis (Figs. 5 and 6). As the length of altitude exposure increased, the excretion of $^{14}\text{CO}_2$ increased, which indicates an enhanced rate of utilization of the available glucose during the exposure period. This may be related to an adaptation to the hypoxic environment that required the synthesis of rate-limiting enzymes in the metabolic pathways of glucose catabolism.

Plasma insulin and growth hormone levels showed minimal significant effects of altitude, possibly due to the small number and large variability of observations. The data were combined for all altitude-exposed men and for all controls to obtain consistent significance for the increased insulin levels after glucagon infusion. These data appear to indicate that post-glucagon elevation of insulin had a greater duration in altitude-exposed men since significant differences were obtained at 20 and 50 minutes after the infusion. Growth hormone was generally increased at altitude, especially in the men studied immediately after altitude exposure; however, no significant differences were noted because two of the men had increases of 8- to 10-fold, while the third had none. Only an occasional 3 to 4 times the control level was noted in men studied after 16 or 40 hours at altitude. Although altitude appears to increase growth hormone, especially during the first few hours of altitude exposure, interpretation of these data is complicated by the large variations between subjects and the fact that the altitude subjects had significantly higher hormone levels at sea level.

CONCLUSIONS AND RECOMMENDATIONS

Although not conclusive, the data obtained in these studies were consistent with the hypothesis that glycolysis was increased at altitude. The elevated catabolism of carbohydrate would explain the earlier observations (1, 2, 18) which indicated that increased carbohydrate consumption improved performance and reduced symptomatology in the abruptly exposed subjects since increasing carbohydrate consumption induces increased activity of the rate-limiting enzymes in its metabolism. The superiority of carbohydrate as a metabolic fuel under hypoxic conditions becomes apparent when one considers that carbohydrate produces 5.05 kcal, while fat produces only 4.87 kcal, and protein 4.48 kcal per liter of oxygen consumed. Another beneficial effect of carbohydrate metabolism under hypoxic conditions, when hyperventilation reduces blood CO_2 content, is that carbohydrate produces 1.00, fat produces 0.71, and protein produces 0.80 liters of carbon dioxide for each liter of oxygen consumed. While

oxygen consumption is only decreased 4.5%, carbon dioxide production is increased 41% in comparing the metabolism of carbohydrate to fat for the same number of kilocalories. The additional carbon dioxide may be required to counteract the losses of the blood's buffering capacity, and this may be more important than the reduced oxygen requirement of carbohydrate metabolism.

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APPENDIX A

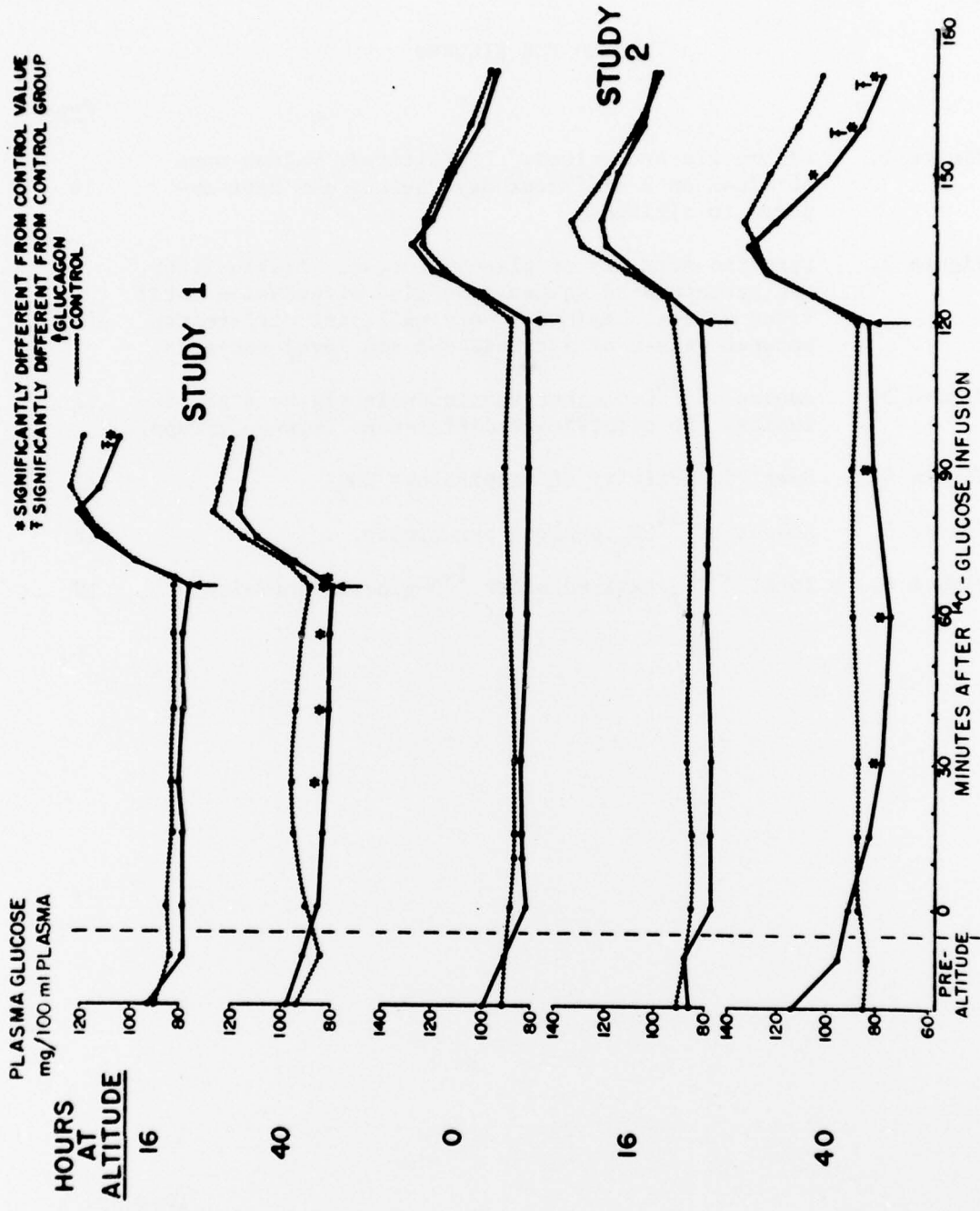


Figure 1

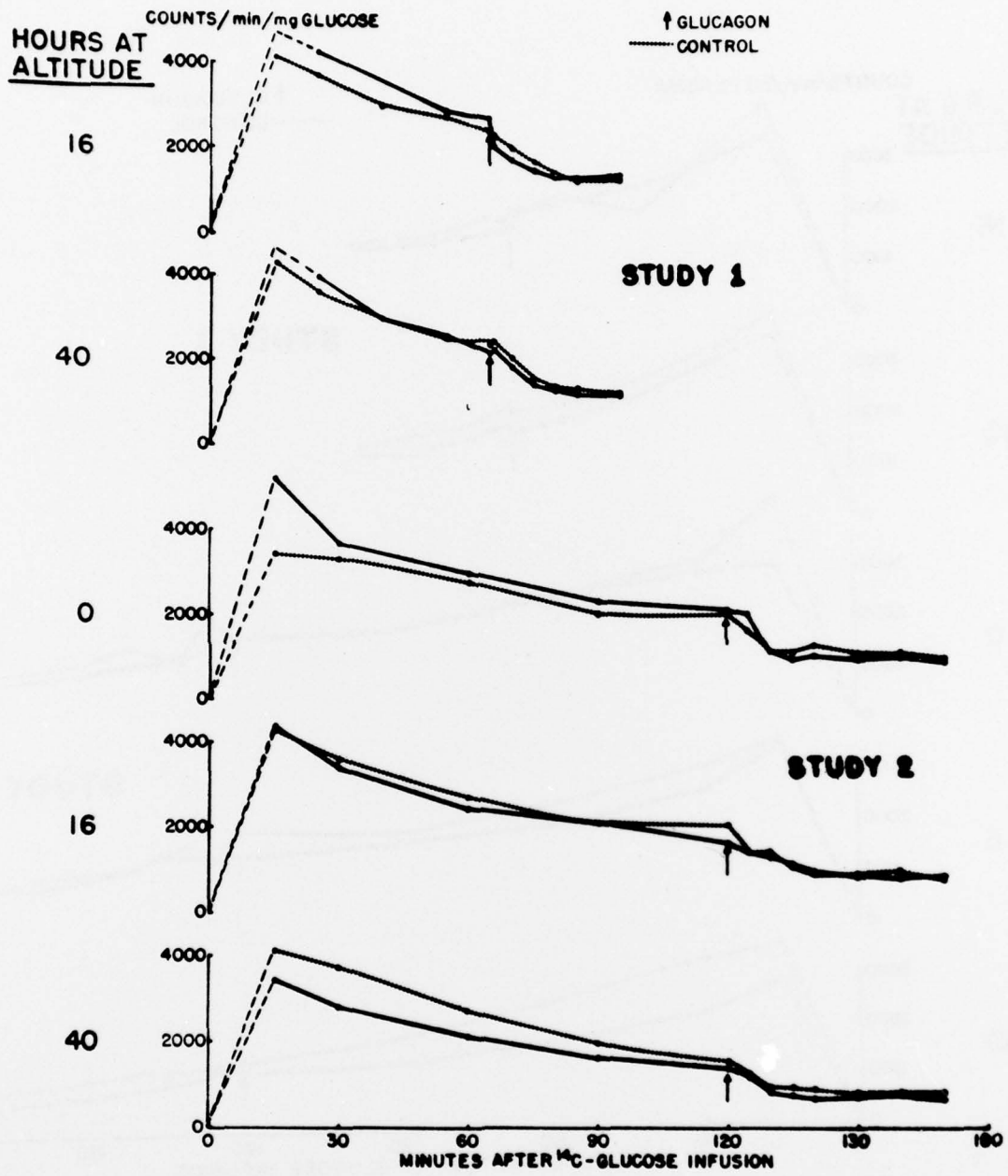


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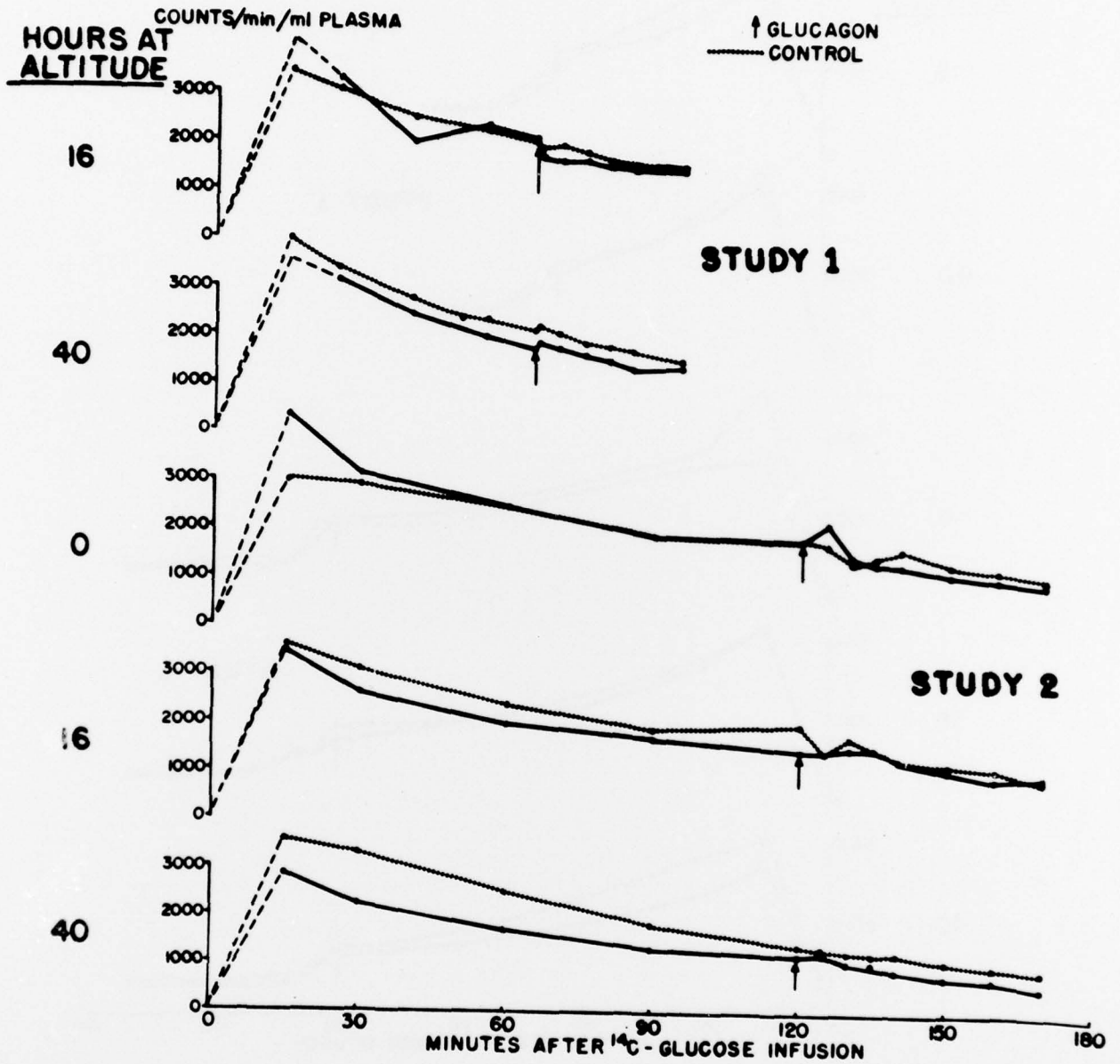


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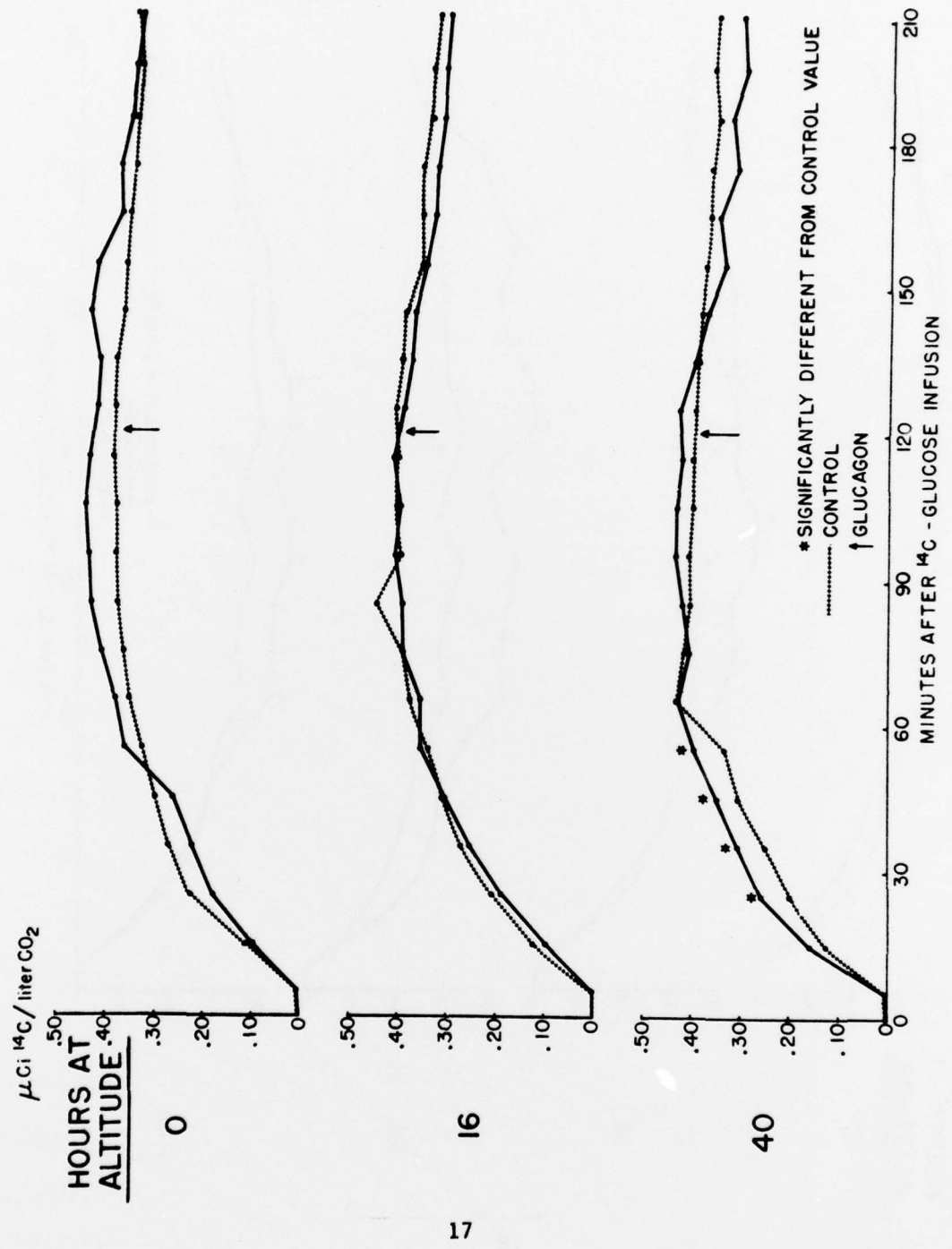


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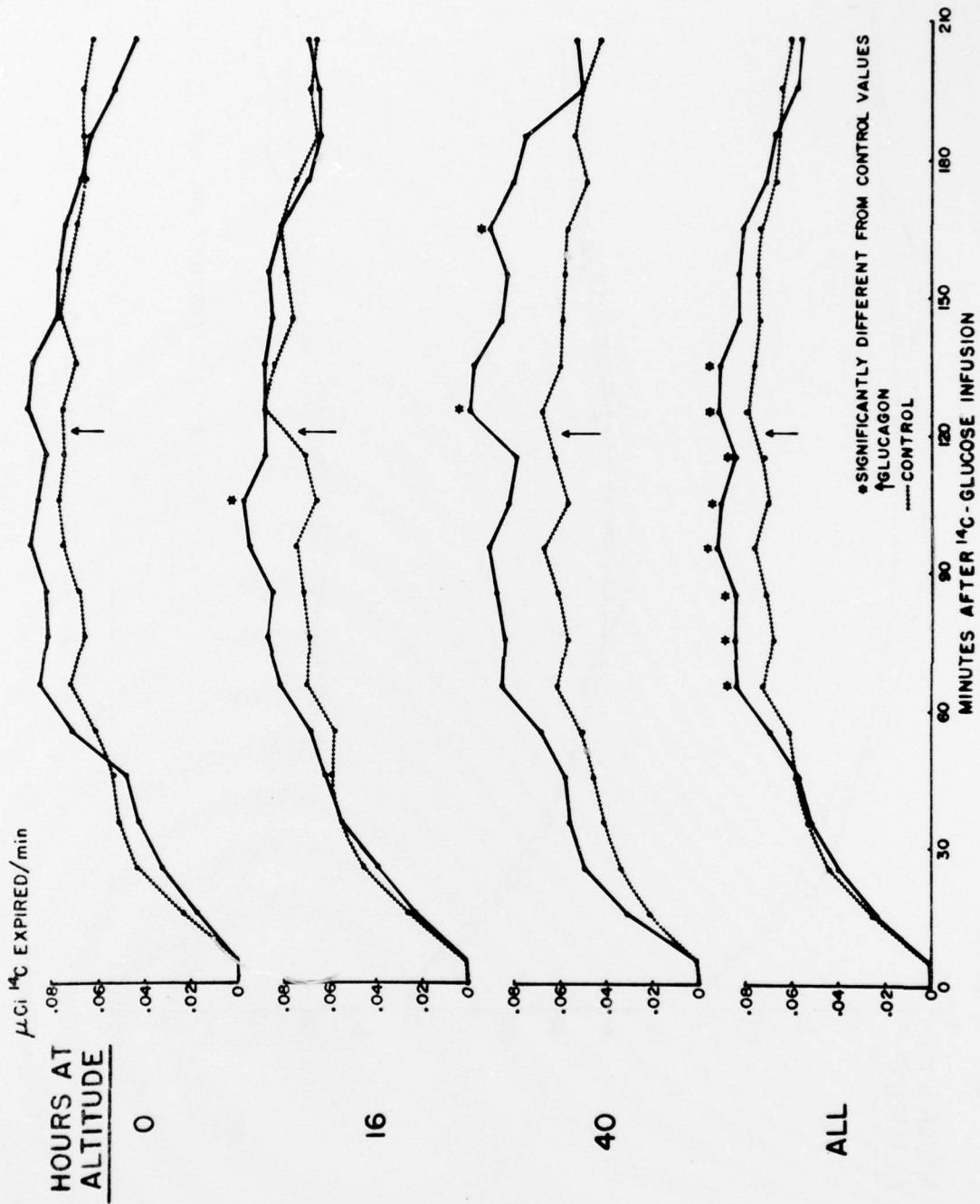


Figure 5

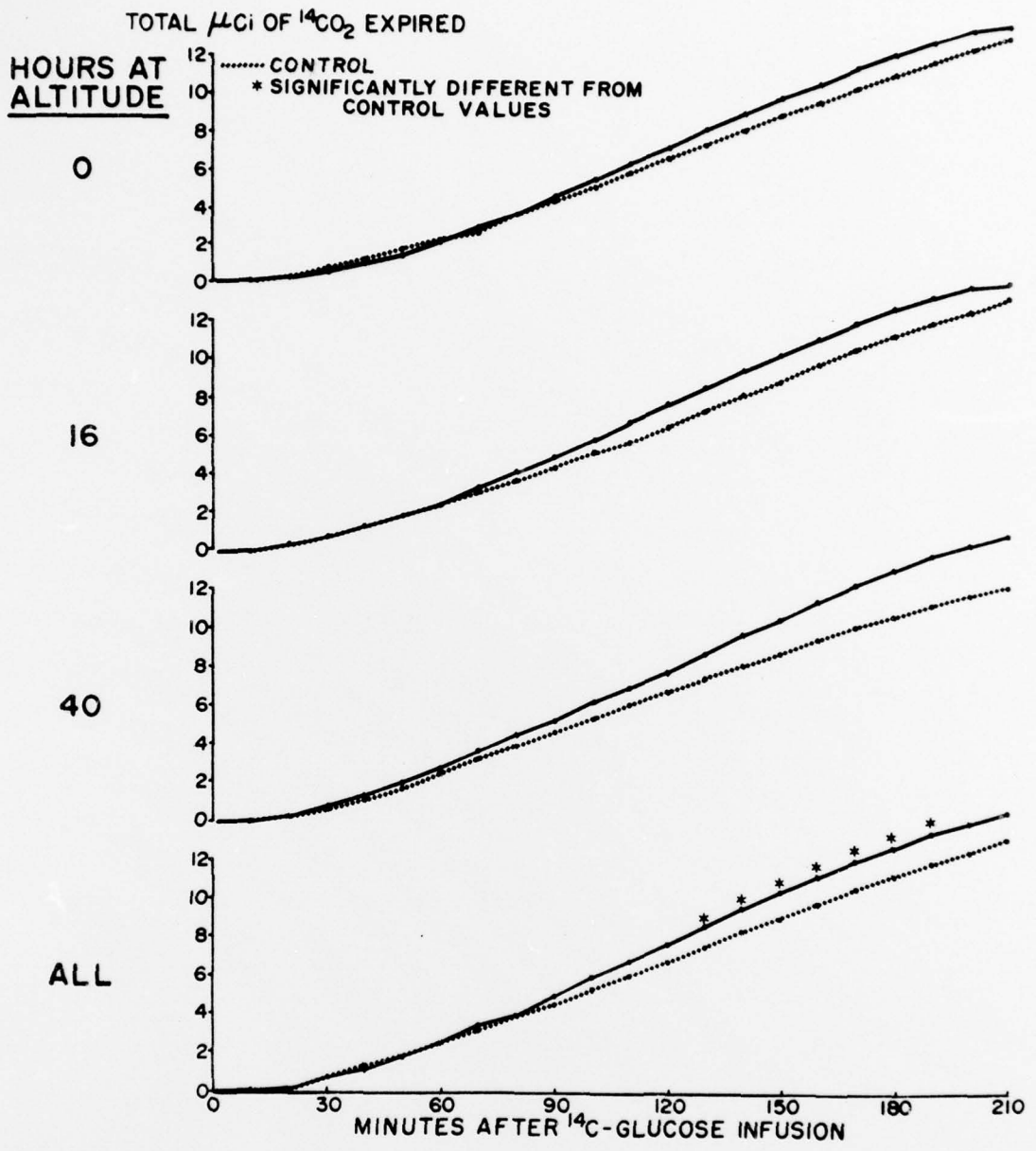


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APPENDIX B

TABLE 1
DIET COMPOSITION

Ingredient	gm/man/day
Meritene ¹	200
Casec ²	45
Sucrose	100
Dextri-maltose ²	140
Corn oil ³	135
NaCl	8
MgCl ₂ .6H ₂ O	2.5
Tween 8-	0.2
Distilled water	<u>1,369.3</u>
Total	2,000

¹D.M. Doyle Pharmaceutical Co., Div. of Dieteen Co., Minneapolis, MN.
²Mead-Johnson Lab, Div. of Mead-Johnson Co., Evansville, IN. ³Best Foods, a Div. of CPC International, Inc., Englewood Cliffs, NJ.

TABLE 2
BODY WEIGHTS OF MEN

Day ^a	Altitude Exposed		Control	
	Av.	SD	Av.	SD
<u>Study I</u>				
-3	69.65	9.44	70.31	8.70
-2	69.76	9.72	70.48	8.52
-1	70.07	9.58	70.46	8.47
0	69.63	9.30	69.87	8.42
1	68.77*	9.29	70.08	8.62
2	68.42*	9.39	69.43	8.48
<u>Study II</u>				
-3	66.94	7.46	71.92	8.50
-2	67.10	7.14	72.03	8.52
-1	67.07	7.21	72.06	8.62
0	67.40	6.98	72.02	8.47
1	66.80*	7.25	72.01	8.38
2	66.70*	6.95	72.00	8.50

^aDays are numbered using day of travel to altitude as Day 0 and equivalent times for control group.

*Significantly different from Day 0 values.

TABLE 3
FOOD INTAKE - kcal/man/day

Day ^a	Av.	SD
<u>Study I</u>		
-1	2963	129
0	2290	397
1	1433	1072
2	2462	779
<u>Study II</u>		
-3	3000	---
-2	3000	---
-1	3000	---
0	2729	504
1	2634	724
2	2543	401

^aDays are numbered using day of travel to altitude as Day 0 and equivalent times for the control group.

TABLE 4
PLASMA INSULIN LEVELS ($\mu\text{U}/\text{ml}$)

Group	Control ^a			Minutes after ¹⁴ C-Glucose Infusion				
	Day 1	Day 2	0	120	125	130	140	170
Altitude	Av. 37.5 ⁽²⁾	26.7	15 ⁽¹⁾	26.3 ^c	34.3	29.7	36.3	23.0
Immediate Exposure (3 men) ^b	SD 30.4	5.5	--	2.1	6.1	8.5	10.4	6.2
Controls (3 men)	Av. 19.3	12.3	22.7	11.3	29.3	26.7	20.3	13.7
	SD 8.5	9.8	14.6	10.0	8.5	8.1	7.0	13.3
Altitude 16-hours (4 men)	Av. 27.0	13.2	25.0 ⁽³⁾	17.5	40.8 ^d	34.2 ^d	40.8	41.7 ⁽³⁾
	SD 13.3	14.2	30.3	11.6	4.8	12.0	24.9	27.4
Controls (4 men)	Av. 13.0	8.0	16.8	21.2	36.2 ^{c,d}	25.5	28.5	19.0
	SD 10.3	5.1	11.4	1.9	12.5	9.3	10.5	12.5
Altitude, 40-hours	Av. 22.7	25.0	40.0 ⁽²⁾	19.3	38.0	38.3 ^d	41.7 ^d	26.7
	SD 8.6	15.6	35.4	4.7	12.3	6.5	5.1	6.7
Controls (3 men)	Av. 21.3	12.3	12.7	15.0	30.3	27.2	28.7 ^d	11.7
	SD 9.1	13.3	10.2	9.2	19.0	18.6	9.9	18.5
Altitude, All 10 men	Av. 27.9 ⁽⁹⁾	20.8	28.3 ⁽⁶⁾	20.7	38.0 ^d	34.1 ^d	39.7 ^{c,d}	30.4 ^{c(9)}
	SD 15.3	13.1	26.7	8.1	7.6	9.3	15.6	16.8
Controls, all 10 men	Av. 17.4	10.6	17.3	16.4	32.4 ^d	26.4 ^d	26.1 ^d	15.2
	SD 9.2	8.6	11.4	7.9	12.6	11.0	9.2	13.4

^aAll control values obtained at sea level (pre-exposure for altitude groups). ^bNumber in parenthesis indicates observations in mean when different than subjects studied. ^cSignificantly different from value of control group. ^dSignificantly different from 120 minute value.

TABLE 5
PLASMA GROWTH HORMONE LEVELS (ng/ml)

Group	Control ^a		Minutes after ¹⁴ C-Glucose Infusion						
	Day 1	Day 2	0	120	125	130	140	170	
Altitude, Immediate Exposure (3 men)	Av.	3.0	3.3	4.0	19.0	16.0	11.3	3.7	
	SD	1.0	1.2	0.0	16.7	16.8	10.7	2.5	
Controls (3 men)	Av.	1.3	1.0	1.3	1.7	3.7	4.7	3.3	3.0
	SD	0.6	0.0	0.6	1.2	2.5	3.2	3.2	2.6
Altitude, 16-hours (4 men)	Av.	4.2 ^b	3.8	5.2	4.0	5.2	5.0	7.8	4.7
	SD	2.5	1.3	3.2	1.4	3.4	0.8	4.6	2.3
Controls (4 men)	Av.	1.0	2.0	2.5	2.2	1.2	2.5	2.5	6.0
	SD	0.0	0.8	1.7	1.0	0.5	2.4	1.9	6.0
Altitude, 40-hours (3 men)	Av.	2.7	3.3 ^b	4.0	3.3	4.0	5.7	4.7	6.0
	SD	1.2	0.6	2.0	2.5	2.6	4.0	2.1	6.2
Controls (3 men)	Av.	2.3	1.7	3.0 ^c	2.0	2.7	2.0	2.0	2.3
	SD	0.6	0.6	0.0	1.0	0.6	1.0	1.0	0.6
Altitude, all 10 men	Av.	3.4 ^b	3.5 ^b	4.5 ^b	8.3	8.1	8.5	7.0 ^{b,c}	4.8
	SD	1.8	1.0	2.2	10.9	8.3	9.7	6.4	3.7

^aAll control values obtained at sea level (pre-exposure for altitude groups).

^bSignificantly different from values of respective control group.

^cSignificantly different from average of control days of same group.

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