TABLE II. Effect of Total of 4 mg RNase IP Injections on Longevity of Mice Bearing Ascites Sarcoma 37.

Group	Days of inj. following inoculation	No. mice	Range of survival, days	Mean survival, days	S.D.	P %
Exp.	2	20	7–16	10.2	2.21	>5
Cont.	2	20	3–17	9.8	2.78	
Exp.	2,3	20	3–18	9.9	3.10	"
Cont.	2,3	18	7–18	10.4	3.01	
Exp.	3,4,5	25	8–19	11.5	2.75	"
Cont.	3,4,5	25	9–15	11.0	2.59	
Exp.	4,5,6,7	25	8–20	11.6	3.70	"
Cont.	4,5,6,7	25	6–14	11.2	3.15	
Exp.	5,6,7	16	6–16	9.6	2.42	"
Cont.	5,6,7	19	5–15	9.6	2.45	
Exp.	6,7	16	7–11	9.0	1.36	"
Cont.	6,7	19	6–13	9.0	2.04	
Exp.	7	19	6–13	9.5	1.66	"
Cont.	7	17	7–16	10.2	2.23	

tabolism of nucleic acids were precipitated by action of RNase.

Summary. 1) Subcutaneous injections of ribonuclease in 5, 10, 20, 40, 80 and 120 mg over an 8-day period do not significantly prolong life of mice carrying ascites sarcoma 37. 2) Intraperitoneal injections of 4 mg RNase over various time periods failed significantly to alter the expected mean survival time of ascites bearing mice.

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Diet Induced Variations in Tolerance to Altitude Hypoxia in the Mouse.* (24794)

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It has been previously shown that changes in the diet modify human tolerance to altitude hypoxia. King *et al.*(1) have reviewed these studies and noted that a high carbohydrate diet results in better visual, psychomotor and psychological performance at altitude. High protein or high fat meals tended to produce reverse effects. Kosmolinskiy(2) indicates that in man a combination of water-soluble vitamins also leads to increased resistance and a heightened sense of well-being. Both Craven *et al.*(3) and Campbell(4) have shown that rats fed exclusively on carrots had prolonged survival times in the altitude chamber. Interest in the physiological deficit produced by lipemia has prompted studies on relationship of fat intake to defects in oxygenation. Mosinger and Kuhn(5) studied effects of oxygen lack in mice fed large amounts of fat. They gave olive oil and isocaloric amounts of starch to their animals and demonstrated sig-

* The contents of this article reflect the personal views of the authors and are not to be construed as statement of official Air Force policy.

nificantly decreased survival times in oil-fed animals compared to controls and those fed starch. These results were interpreted to demonstrate that relative hypoxia plays a role in the circulatory abnormalities produced by lipemia. The present studies were conducted in an attempt to confirm and extend observations on effects of diet on resistance to hypoxia.

Methods and materials. Male mice of the Hamilton Laboratory strain, weighing between 18 and 28 g, were used. Before delivery to this laboratory they were fed the Rockland mouse diet, and at this laboratory were given Purina Laboratory Chow† at least 5 days prior to use. For purposes of the experiment, fasting mice had been given only water *ad libitum* for about 18-20 hours prior to intubation with the experimental feed. The latter was given intragastrically through a soft polethylene catheter after the animal had been transiently anesthetized with ether. It was usual for the animal to be awake and active directly after feeding. Non-fasting mice were allowed to eat *ad lib.* before and after intubation. One of the following materials was given to an experimental group, in amounts noted 10 g of body weight: water, olive oil, corn oil or coconut oil, 0.2 ml; a suspension of 10.5 g of starch and 10.5 g of sucrose in 12.5 ml of water, 0.2 ml, 0.4 ml, or 0.6 ml; a solution containing 10.5 g sucrose in 12.5 ml of water, 0.4 ml; an emulsion containing equal parts of olive oil and the sucrose solution, 0.4 ml; a suspension of 2.5 g of Casec in 10 ml of water, 0.4 ml. Four hours later the animals were placed in the altitude chamber, except for certain groups which were made hypoxic at different times; these are noted in Table I. The altitude chamber consisted of a desiccating jar the interior of which was divided into 4 compartments, each holding one animal. The chamber was evacuated within 65 seconds with Cenco-Hyvac pump to a pressure of 196.3 mm Hg (33,000 feet, true altitude). This measurement was made with a mercurial altitude test barometer (Haas Bros. Instrument Co.). At this time, a stop watch was started and the animals observed closely. The time when each animal took its last breath was noted. The elapsed seconds were then recorded as survival time at altitude. Estimates of this time by 2 independent observers agreed within 5 seconds. In another experiment, 2 groups of 8 fasting mice were fed olive oil and sucrose solution respectively. Another similar group remained fasting. Four hours later serum was prepared from each animal and the sera within each group pooled. The pooled sera were then analyzed for total esterified fatty acids by the method described by Stern and Shapiro(6).

TABLE I. Effect of Various Nutrients on Tolerance to Altitude Hypoxia in the Mouse.

Material	No. of mice	Time between feeding and exposure, hr	Mean survival time, sec. ± S.D.
Corn oil	14	4	47 ± 14
Coconut oil	15	4	65 ± 20
Olive "	14	4	59 ± 28
" "	24	7	61 ± 26
Water	21	4	50 ± 13
Normal diet*	17	4	101 ± 44
Normal diet + olive oil*	16	4	109 ± 53
Normal diet + Casec*	12	4	122 ± 50
Normal diet + starch-sucrose* (.4 ml)	16	4	225 ± 82
Starch-sucrose			
.2 ml	12	4	284 ± 194
.4 "	14	4	284 ± 172
.6 "	10	4	275 ± 121
Sucrose	12	½	294 ± 128
"	11	2	270 ± 103
"	21	4	397 ± 156
"	14	6	442 ± 221
" + olive oil	9	4	415 ± 158

* These animals were not fasting prior to experimental feeding.

Results. Table I shows average survival time for each group. All values included in one section of the Table differ significantly ($p > .01$) from those in any other section. Differences noted in comparisons between carbohydrate-fed animals and other groups are highly significant ($p > .001$). The groups within each of the first 2 sections show values which are not significantly different from each other ($p > 0.1$). In the third section, the su-

† Analysis: Crude protein, not less than 23.0%; crude fat, not less than 5.%; crude fiber, no more than 6%; nitrogen free extract, not less than 44%; ash, not more than 9%.

crose at 4 and 6 hours, and the sucrose and olive-oil mixture differ statistically from the normal diet—starch and sucrose combination ($p<.01$).

Eight animals with survival times greater than 3 standard deviations from the mean of their group have been excluded from these analyses. Of these animals, 7 had been fed sugar and had survival times greater than 15 minutes.

For purposes of discussion, the animals fed water only, are called the fasting group. When sucrose, or a starch-sucrose mixture is fed, regardless of the previous nutritional status or the concomitant feeding of another nutrient, the animals lived about 5 or more times longer at altitude than the fasting, or the oil-fed and fasting subjects. They survived more than twice as long as mice placed on any other combination of diets. There appeared to be no difference in survival of animals fed lipids of varying saturations. Carbohydrate uniformly provided protection when given at different times and in different amounts prior to exposure to altitude. The sucrose alone, in the largest doses, and when given at longer times prior to exposure, appeared to be associated with longer survivals.

It is interesting that the fasting group and the groups made lipemic do not differ in tolerance to hypoxia. The mice fed either protein or the laboratory chow have a tolerance between the fasting and the carbohydrate-fed animals.

Analyses for pooled sera of each group for total esterified fatty acids gave the following results: fasting group, 248 mg %; animals fed sucrose, 225 mg %; those fed olive oil, 375 mg %. This indicates that fasting animals were not lipemic prior to exposure to altitude.

Discussion. Survival time of mice made hypoxic in the high altitude chamber is markedly increased by prior feeding of carbohydrate. Neither the fasting animal nor the animal fed fats of widely varying saturations is so protected. In fact, they do less well than animals maintained on their normal diet. These data may be interpreted as indicating a mechanism whereby carbohydrates facilitate utilization of available oxygen. Lipids appear to lack this ability.

That the effects noted do not depend on respiratory quotients associated with nutrients involved, is shown by the observation that mixtures of carbohydrate and fat, or of carbohydrate and the laboratory diet, in which the respiratory quotient is less than one, still give the same protection.

Proposed mechanisms for the salutary effect of carbohydrates have been advanced. Green *et al.*(7) showed that the alveolar oxygen tension of men previously fed carbohydrate and brought to altitude was signicantly greater than that of a group fed a control diet. King *et al.*(1) observed better psychomotor performance in their subjects and related this to increased glycogen reserves which they felt contributed to nourishment of the central nervous system. Van Middlesworth *et al.*(8) noted that rats fasted for 12 hours and then made hypoxic showed an initial hyperglycemia followed by severe hypoglycemia. The hypoglycemic phase did not occur in non-fasting rats, or in fasting rats habituated to hypoxic conditions. Eckman *et al.*(9) found that men fed a high carbohydrate meal had higher arterial oxygen saturations at altitude than controls. In the dog, glucose content of cerebral tissue is lessened during hypoxia, as is arterial blood glucose(10). It is conceivable that under these conditions function of nervous tissue becomes more dependent on available glucose so that hyperglycemia might indeed aid survival.

The possibility exists that lipids exert a detrimental effect on hypoxic tolerance rather than no effect at all. Since we have shown in these studies that fasting animals have survival times as short as those fed lipids, it would appear less likely that this is the case. If, however, the fasting mice were lipemic or became lipemic at altitude, their shortened survival might be a result of this effect and would explain why they behave like the fat-fed animals. The fatty acid analysis indicates that they were not lipemic prior to altitude exposure. De Langen(11) states that at a simulated altitude of about 19,000 feet rabbits develop significant increases in blood lipids.

This did not occur until 24 hours of exposure, however, while the fasting mice in our studies remained at altitude about one minute.

Many changes associated with lipemia, reviewed by Ahrens(12), could contribute to deficient oxygen transport and would lend support to the possibility that fats are in themselves detrimental to tolerance to hypoxia. We must conclude from our data, however, that the apparently adverse effect of a high fat diet on survival of mice exposed to altitude is a result of carbohydrate deficiency rather than lipid excess.

The difference between the results of Mosinger and Kuhn and those presented here may be explained by inclusion in our series of a group of fasting animals and of groups fed sucrose. Although our data do indicate that a diet consisting of fat alone is associated with a significant decrease in survival time, they more clearly reveal the positive role played by carbohydrate.

Summary. Mice fed large amounts of carbohydrate prior to exposure to altitude hypoxia survive at least 5 times longer than fasting animals and significantly longer than animals fed their normal diet. When fed lipids of varying saturations while fasting, their tolerance is the same as that in the fasting state alone. Large amounts of fat added to the regular diet failed to decrease survival. These results demonstrate a salutary effect of carbohydrates on tolerance to hypoxia. They show as well the inability of lipids to alone promote survival. Possible mechanisms for the protection provided by carbohydrate are discussed.

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Amylase in Pancreas, Intestine, Liver, and Serum During Fasting, Non-protein Diet and Realimentation.* (24795)

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Apparently any meal is mixed with so much endogenous protein that in the small gut the resulting amino acid mixture tends to remain constant(1,2,3). This endogenous protein arises primarily from secreted enzymes and glycoproteins, as well as sloughed mucosa, and most of it may be hydrolyzed and recovered by absorption. The mass of mucosal cells entering lumen of alimentary tract in man may be as much as ½ lb/day(4). The alimentary tract obviously contains a fairly large and mobile protein reserve. This was demonstrated by changes in total N content of some abdominal viscera during fasting, non-protein feeding and realimenta-

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