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Factors Affecting the Reaction of Mice to Low Atmospheric Pressures.*

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In the course of work reported previously[1] we observed that mice died immediately after exposure to a sudden reduction of atmospheric pressure to 70 mm. Those that had previously been allowed access to a mixed food showed a marked congestion of the lungs, causing the surface to appear very dark, almost black. Those that had been deprived of food for approximately 24 hours, although they died just as promptly, did not show this darkening or blackening of the lungs.

In the present paper we wish to report on the effect of administering amino acids, protein, fat, carbohydrate, and sodium chloride, separately, upon the incidence of such pulmonary congestion. We have also conducted some experiments in which the mice were allowed to breathe oxygen, oxygen plus 5% carbon dioxide and air plus 5% carbon dioxide for a short time before the exposure to low pressure, and now report upon the effect of various foods upon the proportion of the animals surviving such treatment.

Experimental. White mice of 14 to 20 g were fed a standard commercial food (Fox Food Blox) and were housed in metal cages containing sawdust. Animals of different sexes were kept separately. At 2 p.m. of the day before the tests, mice which had been provided with adequate food and water since the previous day were transferred to cages with wire screen bottoms and subsequently allowed access to water but not to food. These animals were divided into two groups. Some were tested at various times between 20 and 27 hours after being deprived of food, and were found not to develop the characteristic lesions of the lungs. Other animals were either allowed continuous access to food (nonfasting), or, after the fast, were given access to food (fasting plus food) or had the various substances that were to be tested administered, either intragastrically or intraperitoneally as indicated in the tables, before being exposed to low pressure.

The apparatus used and the method of using it were the same as those employed in our previous work. As in the earlier paper, we have designated as "injured lungs" those showing congestion in at least half the surface, and as "completely injured" those in which the entire surface was congested.

By a slight change in the apparatus, various gas mixtures could be circulated through the desiccator containing the mice, for 10 minutes before reducing the pressure. Because the desiccator that we used for these experiments was larger than the one previously used, a pressure of 16 mm of mercury was necessary in the reservoir tanks, and about 30 seconds were required for the entire system to come to 70 mm.

In these experiments with high oxygen tensions, we were careful to use mice which were fairly uniform in weight, since, apart from other factors, smaller animals seemed to show a somewhat higher survival rate. This is in agreement with the experience of other workers.[2] We tested about 90 fasting mice and about 50 mice after feeding for one or 2 hours on the mixed food subsequent to the fast. A smaller number of mice were tested one or 2 hours after the administration of 0.6 cc of olive oil or one hour after the administration of 0.6 cc of 10% glucose. The oil was given by stomach tube, while the glucose was administered either by stomach tube or by intraperitoneal injection. Since the results which were obtained by both methods of administration of glucose were the same, they are combined in Table I.

The sudden fall in pressure did not seem to

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1 Kibrick, A. C., and Goldfarb, A. E., in press.

2 Van Liere, E. J., *Anoxia, Its Effects on the Body*, Chicago, 1942, p. 213.

TABLE I.

	No. of animals	Survivals, %	Dead, No.	With injured lungs, % of No. dead	With compl. injured lungs, % of No. dead
		Oxygen.			
Fasting	90	50	45	40	11
,, + food	55	2	54	100	80
,, + 10% glucose	12	8	11	90	82
,, + olive oil	12	83	2	50	50
Non-fasting	28	18	23	91	61
		Oxygen + 5% CO_2.			
Fasting	49	53	23	26	4
,, + food	46	7	43	98	56
		Air + 5% CO_2.			
,,	24	0	24	8	0
,, + food	18	0	18	72	44
		Without Previous Ventilation.			
,,	48	0	48	12	4
,, + food	44	0	44	96	67

excite the animals, and an interval of several seconds at 70 mm was necessary before they showed signs of discomfort. Some of the surviving mice were killed with ether, and their viscera were examined. Although a few of the animals were found to have developed lesions of the lungs, most of them had no obvious injury in any of their viscera. Once past the day after the tests, the surviving mice gained weight like normal animals and were susceptible in the usual way when again subjected to the low pressure. While we can not be certain, the absence of any apparent injury in the survivors which had received the oxygen would seem to indicate that the fatalities were due to acute anoxia.

That the greater number of survivals in fasting mice previously supplied with oxygen-rich mixtures was not due to the longer time required for the attainment of the low pressure in the larger chamber which was used in these experiments is shown by the figures in the lower part of Table I. Nor, apparently, did this longer interval of time affect the relative number of animals showing lesions in the lungs.

Results. Whereas fewer than 1% of the mice which previously respired in atmospheric air or in air plus 5% carbon dioxide survived exposure to 70 mm,[1] more than half of the fasting mice which previously respired in oxygen or in oxygen plus 5% carbon dioxide for 10 minutes were not killed by this treatment. Campbell[3] found a slightly greater survival rate in fasting rats subjected to diminished pressure for periods of about 30 minutes than in rats which had not been deprived of food. However, his results with fasting rats did not show the marked differences which he found with rats which had been fed carrots exclusively for several days. This is contrary to our own experience with mice exposed to a pressure of 70 mm after previous treatment with oxygen. We have been unable to detect any marked differences between the susceptibility of mice which had been fed exclusively on carrots for 5 to 7 days and that of fasting mice.[4]

This greater resistance to the effects of low pressure was nearly completely abolished by the taking of mixed food or by the administration of glucose. In marked contrast, the proportion of survivors after the administration of olive oil was even greater than among the fasting animals.

In Table II, we present data showing the effect of the administration of various substances upon the incidence of pulmonary congestion in mice exposed to a pressure of 70 mm without previous treatment with oxygen. Slightly different results were obtained with the 2 series of mice that were allowed access to mixed food after the fast. They are, there-

3 Campbell, J. A., *Quart. J. Exp. Physiol.*, 1938, **28**, 231; 1939, **29**, 259.

4 Kibrick, A. C., unpublished.

TABLE II.

Dose: Material	Vol., cc	Route*	Time elapsing between the administration of the substance and the exposure to 70 mm pressure — Minutes / No. of animals	0	5	15	30	45	60	90	120	180	240	300
10% egg albumin	0.6	G	Total			11	6	12	18	12		12	10	
			With injured lungs			2	0	1	0	1		0	2	
			Compl. injured lungs			1	0	1	0	1		0	1	
Olive oil	0.6	G	Total						6		6	11	17	
			With injured lungs						0		0	2	1	
			Compl. injured lungs						0		0	0	0	
10% xylose	0.6	G	Total			6	6		6		6	5	6	
			With injured lungs			0	1		2		1	0	0	
			Compl. injured lungs			0	1		0		1	0	0	
10% alanine	0.6	G	Total			11	6		5	6	6	6	6	
			With injured lungs			8	1		3	3	3	5	2	
			Compl. injured lungs			1	0		1	1	1	3	2	
10% leucine	0.6	G	Total			6	6		9		6	6	12	
			With injured lungs			3	1		2		1	2	1	
			Compl. injured lungs			3	1		0		0	2	0	
0.9% NaCl	0.6	G	Total			6	6		6		6	6	12	
			With injured lungs			0	0		0		1	0	3	
			Compl. injured lungs			0	0		0		0	0	0	
3% NaCl	0.6	G	Total			12	6		6	6	6	12	12	
			With injured lungs			0	0		0	1	3	0	1	
			Compl. injured lungs			0	0		0	1	1	0	1	
0.9% NaCl	0.6	P	Total				6		6		5	6		
			With injured lungs				0		0		0	0		
			Compl. injured lungs				0		0		0	0		
1 or 2 hr feeding of Fox Food Blox			Total	24			10		18		12	12		
			With injured lungs	24			10		18		12	4		
			Compl. injured lungs	20			7		16		11	2		
1 or 2 hr feeding of Fox Food Blox			Total	24			10		18		12	18	17	
			With injured lungs	24			10		18		12	16	9	
			Compl. injured lungs	21			9		15		10	13	7	
10% glucose	0.6	G	Total		6	12	6	6	19		8	8		
			With injured lungs		3	8	6	4	14		7	3		
			Compl. injured lungs		0	6	5	2	9		6	0		
,, ,,	0.6	G	Total				6		12	6	12	16	6	5
			With injured lungs				6		12	4	8	12	6	1
			Compl. injured lungs				5		10	2	5	8	3	0
,, ,,	0.6	P	Total			6	12		11	12	11	6	6	
			With injured lungs			3	10		4	9	11	5	4	
			Compl. injured lungs			0	7		1	7	4	3	3	
10% starch	0.6	G	Total		6	18	18	6	18	6				
			With injured lungs		2	10	12	4	9	0				
			Compl. injured lungs		2	6	4	2	2	0				
,, ,,	0.6	G	Total			6	6		6	6	6	6	6	6
			With injured lungs			2	5		6	5	5	6	4	2
			Compl. injured lungs			1	3		2	3	1	2	0	1

Material		Hours of fast / Number of animals: 20	21	22	24	26	27
None	Total	36	18	36	36	25	18
	With injured lungs	8	1	4	4	4	2
	Compl. injured lungs	3	1	2	1	1	1

* G = intragastric. P = intraperitoneal.

fore, presented separately. Somewhat different results were also obtained with the 2 series of mice which received glucose or starch by stomach tube.

As may be seen from the table, only starch and glucose acted as did the mixed food in increasing the proportion of mice showing injured lungs, and glucose had this effect whether it was given intragastrically or intraperitoneally. Just as in the mice that were previously treated with oxygen, the action of olive oil seemed to protect against injury, rather than sensitize to it.

Summary. Mice that had been permitted access to a mixed food before exposure to high tensions of oxygen with a subsequent sudden fall of total pressure to 70 mm were found much more likely to succumb to such treatment than were mice that had been deprived of food for a day. This effect of food was also observed after the administration of glucose, intragastrically or intraperitoneally, but not after the intragastric administration of olive oil.

Mice not previously treated with high tensions of oxygen were nearly all killed by the sudden exposure to 70 mm pressure, but those that had been deprived of food did not show the marked congestion of the lungs that was observed in mice that had been fed a mixed food. Mice that had received glucose or starch showed this congestion, but those that had received xylose, olive oil, egg albumin, leucine, or sodium chloride did not.

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Studies on Rates of Hydrolysis of N^4 Dibasic Acid Substituted Sulfonamides.*

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The reports of Poth, Knotts, Lee and Inui[1] and Poth and Ross[2] detailed the results of a study of 33 sulfonamides which were examined for bacteriostatic activity in the gastrointestinal tract. Fourteen of these compounds were N^4 acyl (dibasic acid) derivatives. Succinylsulfathiazole and phthalylsulfathiazole, of this series, have been shown to possess considerable local bacteriostasis in the gastrointestinal tract and were studied extensively both experimentally and clinically.[3-11]

Many of the other members of this series were found to have little antibacterial activity in the bowel. Since the conjugated sulfonamides have but slight bacteriostatic activity, the simplest explanation of the activity of these compounds should be due to the free sulfonamides liberated by the hydrolysis of the acylated compounds. If this were true, then the rates of hydrolysis of these sulfonamides in aqueous solutions of varying hydrogen ion concentrations should furnish an index to their antibacterial activity.

Poth, Knotts, Lee, and Inui[1] observed that

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