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The Significance of Changes in Adrenal Size After Periods of Anoxia in Rats.*

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It has been shown that enlargement of the adrenals occurs after periods of exposure to decreased atmospheric pressure.[1-4] Lawless[5] demonstrated an increase in the water content of the adrenals of rats exposed to a pressure of 254 mm Hg (28,000 ft) for 3½ hr. He suggested that the increased water might be associated with augmented adrenal activity.

In this laboratory, histological examination of the adrenals of rats sacrificed after decompression to 225 mm Hg (30,000 ft) for periods up to 24 hr revealed hyperemia and congestion concomitant with an increase in size. The glands of those animals surviving the longer periods of decompression at this pressure also showed necrosis, cellular atrophy and edema. It was decided, therefore, to determine whether the weight gain of the adrenals might be due to the increased blood content.

Male albino rats were weighed and placed in vacuum desiccators which were evacuated by water aspirators. The animals were brought to an equivalent altitude of 30,000 feet at the rate of 1500 ft per min. The pressure was maintained within 2 mm by a mercury valve. Food and water were withheld during the experiment. At the close of the decompression period, the animals were brought to atmospheric pressure at the rate of 3000 ft per min, weighed, and sacrificed by a blow on the head. The adrenals were immediately removed, freed from adhering tissues, weighed, and dried to constant weight at 100° C. Blood samples (2 cc) were taken, weighed and dried to constant weight. Control animals were treated in the same manner except that they were not decompressed. The rats were weighed to the nearest gram and the adrenals to the nearest tenth of a milligram. The data were analyzed statistically by means of the "t" test for significance as described by Snedecor.[6] In all of the analyses there were 18 degrees of freedom, hence the t values must be greater than 2.1 or 2.88 to be significant at the 5 or 1% levels respectively.

The results are expressed in the accompanying table. Starvation alone, for the periods in these experiments, produced no effect; therefore, one set of figures, that of the fed controls, is used as a basis of comparison with the experimental values. The water content of the blood, which was 79.0%, did not change.

At the end of 7 hr exposure to anoxia there is an average increase of 0.0028 g in the absolute weight of the adrenals. When this is expressed as grams of adrenal tissue per 100 g of body weight, the increase which is 0.0060 g is statistically significant, t being 4.55. The weight of water contained in the glands has also significantly increased by an average of 0.0024 g, t being 15.77. The percentage of water in the glands has increased 1.9%.

The adrenals of animals exposed to anoxia for 24 hr show a decrease of 0.0029 g in weight. Despite this loss in absolute weight there is a slight gain of 0.0002 g per 100 g of body weight. This increase is statistically insignificant, t being 0.18. The actual weight of water has decreased but the percentage of

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1 Earlier work reviewed by Tepperman, J., Engel, F. L., and Long, C. N. H., *Endocrinology*, 1943, **32**, 373.

2 Sundstroem, E. S., and Michaels, G., *Memoirs of the Univ. of Calif.*, 1942, **12**, Univ. of Calif. Press, Berkeley.

3 Darrow, D. C., and Sarason, E. L., *J. Clin. Invest.*, 1944, **23**, 11.

4 Tornetta, F. J., Gordon, A. S., D'Angelo, S. A., and Charipper, H. A., *Fed. Proc. Amer. Soc. Exp. Biol.*, 1943, **2**, 50.

5 Lawless, unpublished work quoted in Van Liere, E. J., "Anoxia," 1942, p. 206, U. of Chicago Press, Chicago, Ill.

6 Snedecor, G. W., *Statistical Methods*, 1940, The Iowa State College Press, Ames, Iowa.

TABLE 1.
Effect of Anoxia on Adrenals.
(Avg. and range: 10 rats on each point.)

		Body wt g	Adrenal wt g	Adrenal wt g per 100 g body wt	Water wt g	Water content %
Controls	Fed	176.6	0.0271	0.0159	0.0181	66.9
		(131-228)	(0.017-0.039)	(0.010-0.022)	(0.011-0.026)	(63.9-72.0)
	Starved 7 hr	161.9	0.0270	0.0168	0.0180	66.9
		(149-200)	(0.020-0.035)	(0.010-0.020)	(0.014-0.023)	(63.5-69.0)
	" 24 "	159.1	0.0265	0.0167	0.0177	66.8
		(147-174)	(0.024-0.029)	(0.014-0.018)	(0.016-0.020)	(64.3-68.4)
	Anoxic 7 "	140.6	0.0299	0.0219	0.0205	68.6
		(128-154)	(0.022-0.034)	(0.019-0.027)	(0.015-0.024)	(62.1-73.0)
	" 24 "	151.1	0.0242	0.0161	0.0166	68.6
		(135-175)	(0.022-0.028)	(0.015-0.019)	(0.015-0.020)	(58.3-78.5)

water is still elevated over that of the controls.

It may be seen, therefore, that at the end of 7 hr exposure to anoxia there is an increase in weight of the adrenals which amounts to 0.0060 g per 100 g of body tissue. The water in the adrenals of the control animals amounted to 0.0106 g per 100 g of body weight (0.0159 $\times$ 0.669). In the 7-hr group the water content has risen to 0.0150 g per 100 g of body weight, an increase of 0.0044 g per 100 g of body weight. If the increase in weight were due to an increased blood content, the figure 0.0044 would represent only 79.6% of the weight of the blood, as 20.4% would be solid matter which would not be lost by drying. This residue would, therefore, amount to 0.0011, thus accounting for 0.0055 of the increase of 0.0060 g per 100 g of body weight.

It is also evident that at the end of 24-hr exposure to anoxia there is an absolute loss of adrenal weight. This is probably due to a loss of tissue, since the water content has actually increased and histological examination reveals areas of necrosis, exhaustion atrophy and edema.

These results indicate that the immediate response of the adrenal to anoxia is hyperemia. It is suggested that, perhaps, this occurs as a result of other forms of stress. Observations on wet weights alone, made at an early stage would give a false impression of hypertrophy. The augmented blood supply is probably an indication of hyperactivity. Evidence of an increased demand for adrenal cortical factors has been offered by others[1,3] and by Dr. K. A. Brownell in unpublished observations on the effects of anoxia on carbohydrate metabolism made in this laboratory. Continued exposure to the decreased oxygen tension at 30,000 feet causes exhaustion atrophy of the cortical cells of the adrenal.

Acclimatization to an equivalent altitude of 30,000 ft has not been demonstrated. It is highly probable that, at altitudes at which acclimatization can occur, the adrenals would show hyperemia but would not undergo exhaustion atrophy. Instead, it is felt that recovery followed by true hypertrophy as evidenced by a gain in dry weight would occur. When the question of hypertrophy of the adrenal is being considered, it is important to determine wet and dry weights of the gland to ascertain whether the observed weight gain is due to hyperemia or is caused by an increase in solids. As lipids appear to play so dominant a role in adrenal cortical activity, it would be valuable to determine the changes in these substances.

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Summary. Evidence is presented to show that the weight increase of the adrenals of rats exposed to a pressure of 225 mm Hg for 7 hr is due to hyperemia, indicating hyperactivity of the gland in response to the stress of anoxia. At this reduced pressure, the gland is unable to respond to the body's requirements and undergoes exhaustion atrophy as evidenced by histological examination and wet and dry weight determinations at the end of 24 hr decompression.