13579

Effect of Low Atmospheric Pressure on the Adrenals, Thymus and Testes of Rats.

F. C. DOHAN.

From the George S. Cox Medical Research Institute, University of Pennsylvania, Philadelphia.

Recent metabolic[1-4] and histologic[4] studies indicate that the adrenal cortex plays an important rôle in the response of the mammalian organism to lowered oxygen tension in the inspired air. In addition, an increase in the ratio of adrenal weight to body weight in rabbits exposed to ½ atmosphere for 4 hours daily over a period of weeks has been reported by Armstrong and Heim.[5]

The following experiments demonstrate an increase in the *absolute* weight of the adrenal glands in association with a decrease in weight of the thymus and testes in rats exposed to low atmospheric pressure on more than 2 days. This pattern of response is similar to that found by Selye[6, 7] in animals subjected to other forms of stress ("alarm reaction"). We have also observed that diets of widely varying composition had no significant effect upon this change of weight of the glands.

Methods. Male white rats (Sprague-Dawley) were used. The body weight ranged from 270 to 345 g with the exception of one rat weighing 372 g. After a preliminary observation period of 5 to 10 days during which the animals were fed enough of the special diets indicated below to maintain their body weights, they were placed in a low pressure chamber* for small animals and maintained at the various pressures for various periods. The pressure in the chamber was lowered by a pump and kept at approximately the desired level by means of an accessory inlet valve. This was controlled electrically by a closed mercury manometer connected to the chamber. At the

1 Evans, G., *Am. J. Physiol.*, 1934, **110**, 273.

2 Evans, G., *Am. J. Physiol.*, 1936, **114**, 297.

3 Lewis, R. A., Thorn, G. W., Koepf, G. F., and Dorrance, S. D., *J. Clin. Invest.*, 1942, **21**, 33.

4 Giragozsints, G., and Sundstroem, E., PROC. SOC. EXP. BIOL. AND MED., 1937, **36**, 432.

5 Armstrong, H. G., and Heim, J. W., *J. Aviat. Med.*, 1938, **9**, 92.

6 Selye, H., *Endocrinology*, 1937, **21**, 169.

7 Selye, H., *Canad. M. A. J.*, 1940, **42**, 113.

* The low pressure chamber was kindly loaned to us by Dr. C. N. H. Long and Dr. Gerald T. Evans.

lower pressures used the animals developed cyanosis and dyspnea. The pressure was decreased to a constant level over a period of approximately 5 to 15 minutes. Before the animals were removed from the chamber the pressure was increased to atmospheric level in about 2-5 minutes. No significant effects were noted upon the gland weights of 2 rats kept in the pressure chamber only during these periods of adjustment.

The special diets were a slightly modified form of those described by Reinecke, Ball and Samuels[8] for tube feeding. They contain approximately 300 calories per 100 ml. The protein diet was composed largely of casein and could not be tube fed. The caloric distribution of the diets was calculated to be as follows:

	%	%	%
High carbohydrate diet	P 18	F 10	C 72
" fat diet	P 18	F 81	C 1
" protein diet	P 89	F 10	C 1

Normal adult rats maintained their body weight when offered any one of these diets. When fed by tube, a total of 20 ml per day maintained the body weight when at atmospheric pressure. Special precautions were taken not to induce an alarm reaction by too rapid an increase in the amount of food given by tube.[9] The possible effect of this factor was controlled by (1) tube feeding 2 of the control group with no significant effect upon the gland weights, (2) feeding one experimental group a diet to be eaten *ad libitum* and (3) an experiment with starved animals.

The adrenals, thymus and testes of the rats dying during the period in the low pressure chamber as well as those surviving this period were weighed. The surviving animals were anesthetized with ether and then bled to death. Fisher's small sample technic[10] was used for the statistical analysis of the results.

Results. Details concerning the diet, pressure and survival are given in Table I and the legend of Fig. 1. The gland weights are charted in Fig. 1. The probability that the differences in the means of the experimental groups from those of the control group (A) were due to chance is indicated in Table II, in which we have taken as significant those differences for which the probability of occurrence by chance is not greater than 0.05. It is evident that groups C, D and E show a significant increase in mean adrenal weights and decrease in

8 Reinecke, R. M., Ball, H. A., and Samuels, L. T., PROC. SOC. EXP. BIOL. AND MED., 1939, **41**, 44.

9 Ingle, D. J., *Endocrinology*, 1941, **29**, 838.

10 Fisher, R. A., *Statistical Methods for Research Workers*, Oliver and Boyd, London, 1938.

TABLE I.
Survival, Diet and Pressure.

		Number of rats dying on day and at pressure indicated*							
Group C (11 rats)	Day	1	2	3	4	Survived			
	Pressure†	355	315	275	255-235				
Diet: Tube fed	CHO		3			2			
2 × 10 ml daily	Fat		1		1	4			
Group D (6 rats)	Day	1	2	3	Survived				
	Pressure	293	293	293					
Diet: Tube fed	CHO	2			1				
1 × 13 ml daily	Fat	2		1					
Group E (7 rats)	Day	1-2	3-7	8-9	10	11	12	13	Survived
	Pressure	380-340	300	275	255	255	235	235	
Diet: ad libitum	CHO							1	2
	Fat							1	1‡
	Protein				2				

*Groups C and D were in the low pressure chamber 22 to 23 hours daily. Group E was in the chamber about 15½ hours daily. The diet was offered only when out of the chamber.
†Pressure in mm of Hg.
‡Sacrificed on 13th day.

mean thymic weights. The differences of the mean weight of the testes from that of the control group is significant in all except

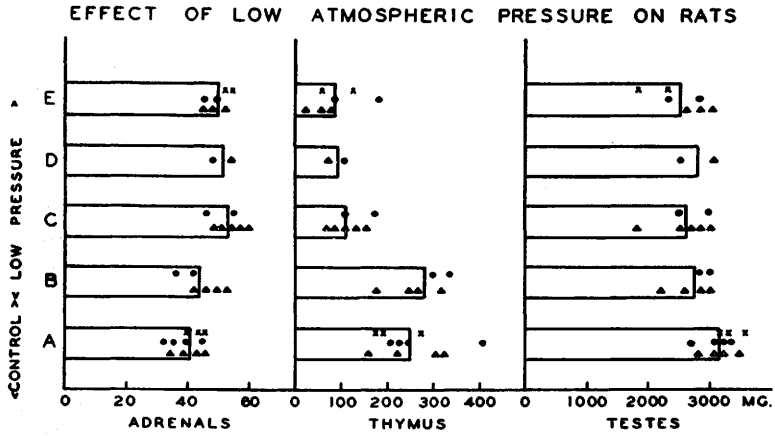

FIG. 1.

Gland weights in rats receiving:
● = high carbohydrate diet
△ = high fat diet
× = high protein diet

Group A—Control group. Atmospheric pressure. Diets eaten *ad libitum* except for 2 rats fed by tube.

Group B—Is composed of rats in Group C and Group D of Table I which died within 2 days after placing in low pressure chamber. Two of the rats in Group C (Table I) which died on the 2nd day were discarded without weighing the glands.

Group C—In this figure only those rats of Group C, Table I, which survived longer than 2 days are charted.

Group D—In this figure only those rats of Group D, Table I, which survived longer than 2 days are charted.

Group E—Same as Group E, Table I.

TABLE II.
Probability That the Difference Between Mean Organ Weights Shown in Fig. 1 Might Have Occurred by Chance.

Group	Glands	Diff. of means of organ wts, mg	Stand. error of diff., mg	Probability of chance occurrence of diff.,* P
B-A	Adrenals	+ 3.7	2.3	>.10†
	Thymus	+ 37	34.3	>.20†
	Testes	—430	124	<.01
C-A	Adrenals	+ 13.1	2.1	<.01
	Thymus	—146	30.2	<.01
	Testes	—570	148	<.01
D-A	Adrenals	+ 15.5	3.4	<.01
	Thymus	—155	53.4	<.02
	Testes	—330	192	>.10†
E-A	Adrenals	+ 10.0	1.8	<.01
	Thymus	—158	33.2	<.01
	Testes	—600	149	<.01

*From Fisher's table of t values.
†Difference not statistically significant.

Group D, consisting of only 2 rats. Those animals dying within the first 48 hours (Group B) do not show a significant deviation of the adrenal or thymus gland weights from the control group. However, the difference in the weight of the testes is significant.

The distribution of the data (Fig. 1) does not indicate a significant *effect of diet* upon the gland weights either at atmospheric pressure or below; nor could any differential effect of diet upon survival be obtained from analysis of our small number of data (Table I). Thus, combining the results in Groups C and D, 3 of 8 rats fed high

TABLE III.
Effect of Atmospheric Pressure of Approximately 300 mm Hg. for 3 to 5 Days upon Gland Weights of Starved Rats.

Glands		No. of rats	Mean gland wt, mg	Stand. error of diff. of means, mg	Probability of chance occurrence of diff.*
Adrenals	Control	6	36.9	4.1	<0.02
	Experimental	5	48.6		
Thymus	Control	6	200	15.6	<0.01
	Experimental	5	81		
Testes	Control	6	2934	87	<0.05
	Experimental	5	2719		

*From Fisher's table of t values.

carbohydrate and 4 of 9 rats fed high fat diets survived until the end of the experiments. *In starved animals* a statistically significant qualitatively similar effect upon gland weights has also been obtained (Table III).

Attempts were made to determine the effect of adrenal cortical extracts† upon the change in the adrenal weights. The results were inconclusive using subcutaneous injections as high as 5 cc twice daily.

Discussion. The above data indicate a definite effect of prolonged exposure to low atmospheric pressure upon the absolute weights of the adrenal, thymus and testes. The pattern of change and the general condition of the animals was similar to that which may be produced by cold, injections of formalin or morphine, severe muscular work and other forms of stress (alarm reaction of Selye[6, 7]). The effect of diet upon prevention or amelioration of the "alarm reaction" due to other agents has not been reported. However, in connection with the lack of effect of diet in our experiment it is well to point out the long time intervals between feedings.

Summary. Rats exposed to low atmospheric pressure for more than 2 days exhibited a significant increase in adrenal weight and a significant decrease in the weight of the thymus and testes. This pattern is similar to that found following other forms of stress. No significant effect of diet upon this change was demonstrated.

13580 P

A Method for Inducing Limb Regeneration in Adult Anura.

S. MERYL ROSE. (Introduced by Otto Glaser.)

From the Department of Biology of Amherst College.

It has been demonstrated by Barfurth[1] and confirmed by subsequent investigators that frogs apparently lose their ability to regenerate limbs during the tadpole stage. On the other hand, a few adult frogs[2] and toads[3] have been observed with very definite indications of limb regeneration. These few cases of regeneration in adults are rare. Usually the stumps heal without regenerating.

† We are indebted to Dr. George F. Cartland of the Upjohn Company for the adrenal cortical extract.

1 Barfurth, D., *Arch. f. Entw.-Mech.*, 1894, **1**, 117.

2 Gadow, H., *Amphibia and Reptiles*, The Cambridge Natural History Series, 1901.

3 Woodland, W. N. F., *Q. J. M. S.*, 1921, **65**.