

the meaning of the fluctuations in the values, especially of the neutral sulfur, can be derived therefrom. The animals showed unmistakable symptoms of intoxication on the days of feeding of brom-benzene, such as depression, loss of vitality and even prostration.

The isolation of phenylmercapturic acid from the urine of fasting growing dogs seems to indicate that the body tissues are capable of supplying cysteine for the detoxication of brom-benzene, even under such drastic conditions as employed by us.

Summary. 1. Brom-benzene was fed to growing dogs which were fasted for 4-5 weeks prior to the administration of brom-benzene. 2. Mercapturic acid was isolated from the urine of pups on the day following the feeding of brom-benzene and identified by analysis. 3. Fasting growing dogs apparently are capable of supplying cysteine for detoxication purposes at the expense of tissue.

8276 C

Effect of Anterior Hypophysis Emulsion on Natural Resistance of Hypophysectomized and Normal Rats to Histamine Poisoning.

DAVID PERLA.

From the Laboratory Division of Montefiore Hospital, New York City.

In previous work we studied the effect of partial and complete hypophysectomy in rats on the natural resistance to histamine poisoning and correlated the anatomical changes in the suprarenal gland with the variations in resistance.¹ We noted that the natural resistance of completely hypophysectomized rats to histamine poisoning was depressed during a period of one to ten weeks after operation. The M.L.D. was one-fifth to one-third that for normal rats. This decrease in resistance, we found, was associated with involutinal changes of the suprarenal gland, such as hemorrhage into or atrophy of the inner zones of the cortex.² Rats in which the posterior lobe and a large portion of the anterior lobe were removed showed a similar drop in resistance and atrophic changes in the suprarenal cortex occurred, but where a large fragment of the anterior lobe remained no depression in resistance to histamine occurred and the suprarenal glands were normal. We concluded that the drop in

¹ Perla, D., and Rosen, S. H., *Arch. Path.* In press.

² Perla, D., *Proc. Soc. Exp. Biol. and Med.*, 1935, **32**, 655.

natural resistance following hypophysectomy in the rat was probably secondary to the atrophic changes of the suprarenal cortex induced by the withdrawal of the adrenotropic hormone of the anterior lobe.

In subsequent studies it was found that repeated injections of large amounts of suprarenal cortical hormone raised the natural resistance of totally hypophysectomized adult rats to histamine poisoning. In some instances the resistance was raised almost to the level of normal rats. This was particularly marked during the first 2 weeks after operation, the period during which the most severe depression in natural resistance occurs. The M.L.D. of histamine for hypophysectomized rats within 2 weeks after operation varied from 200 to 300 mg. per kg. of body weight. Hypophysectomized rats treated with cortical hormone for 6 days prior to the injection of histamine survived, in many instances, 800 mg. of histamine per kg. of body weight.

These observations tended to support the hypothesis that the depression in natural resistance following hypophysectomy was due to the impairment of the function of the suprarenal cortex resulting from the withdrawal of the adrenotropic hormone of the anterior lobe.

In the present communication the effect of repeated injections of a crude emulsion of the anterior lobe of the hypophysis of the ox on the resistance of hypophysectomized and normal rats to subsequent injections with histamine was studied.

All the rats used in these experiments were 3 to 4 months old and of a uniform stock raised in our laboratory for many years. Twenty-eight rats were hypophysectomized, then divided into 2 groups. Nineteen were treated daily with 1 cc. of crude saline emulsion of fresh ox anterior hypophysis; 9 were untreated. At the end of 14 days all were injected with varying amounts of histamine. Those rats treated with emulsion were given histamine in amounts ranging from 400 to 800 mg. per kg. of body weight. Those that were not treated were injected with histamine in amounts ranging from 200 to 600 mg. per kg. of body weight. Three normal controls received 900 and 1000 mg. of histamine per kg. It will be seen from Table I that the natural resistance of hypophysectomized rats treated with anterior hypophyseal emulsion to histamine poisoning was raised considerably. These rats gained greatly in weight and atrophy of the glands of internal secretion and visceral organs did not occur. In many instances the rats survived 700 to 800 mg. of histamine per kg. of body weight. The M.L.D. for untreated hypophysectomized young adult rats varied from 200 to 300 mg. of

TABLE I.
Effect of Repeated Injections of Anterior Hypophyseal Saline Emulsion on the Natural Resistance of Hypophysectomized Albino Rats to Histamine Poisoning (Ergamine Acid Phosphate).

No. Rats	Amt. histamine per kg.	Survived	Died
Hypophysectomized rats treated with anterior hypophyseal emulsion.*			
2	400	2	0
7	600	4	3
4	700	3	1
6	800	1	5
Hypophysectomized rats untreated.			
3	200	1	2
3	300	0	3
3	400	0	3
1	600	0	1
Untreated normal controls.			
2	1000	0	2
1	900	1	0

* The treated rats received 1 cc. of a saline emulsion of ox anterior hypophysis. An emulsion of the anterior lobes of 8 glands was made in 80 cc. of physiological salt solution under aseptic conditions. Fresh emulsion was prepared every third day. Injections were administered subcutaneously in amounts of 1 cc. per rat per day for a period of 14 days.

histamine. Rats treated with pituitary emulsion showed none of the usual effects of hypophysectomy.

Further experimentation, however, will be done to determine what fraction of this crude emulsion is responsible for the increase in resistance of hypophysectomized rats. From data previously obtained it is suggested that the adrenotropic fraction in this emulsion may be a protective factor.

The effect of emulsions of anterior hypophysis (ox) on the natural resistance of normal rats to histamine was determined in a second experiment. Twenty-six adult albino rats, 3 to 4 months of age, were divided into 2 groups. Sixteen received daily subcutaneous injections of a saline anterior hypophyseal emulsion in amounts of 1 cc. per rat per day for a period of 2 weeks. Ten were untreated. All were injected with histamine (ergamine acid phosphate) in amounts varying from 900 to 1600 mg. per kg. of body weight. In previous work³⁻⁷ the M.L.D. of this drug in the normal animals of our stock was found to be about 900 to 1,000 mg. per kg. Only an occasional rat sur-

³ Marmorston-Gottesman, J., and Gottesman, J., *J. Exp. Med.*, 1928, **47**, 503.

⁴ Perla, D., and Marmorston-Gottesman, J., *Am. J. Phys.*, 1929, **89**, 152.

⁵ Perla, David, and Marmorston-Gottesman, J., *PROC. SOC. EXP. BIOL. AND MED.*, 1931, **28**, 650.

⁶ Marmorston-Gottesman, J., and Perla, D., *PROC. SOC. EXP. BIOL. AND MED.*, 1931, **28**, 1022.

⁷ Perla, D., *PROC. SOC. EXP. BIOL. AND MED.*, 1934, **81**, 982.

vived one killing dose of histamine. These rats increased markedly in weight, and at autopsy the suprarenals showed striking hypertrophy as did the gonads, spleen and thyroid. Nevertheless this was not associated with an increase in the natural resistance to histamine. The natural resistance of normal rats was not appreciably raised by repeated injections of a saline emulsion of anterior hypophysis.

TABLE II.
Effect of Repeated Injections of Anterior Hypophyseal Saline Emulsion on the Natural Resistance of Normal Rats to Histamine Poisoning (Ergamine Acid Phosphate).

No. Rats	Amt. Histamine per kg.	Survived	Died
Normal rats treated with anterior hypophyseal emulsion.*			
6	1100	2	4
6	1200	1	5
3	1400	0	3
1	1600	0	1
Normal rats untreated.			
2	900	2	0
4	1000	2	2
4	1100	1	3

* The emulsion was prepared as in the previous experiment. Subcutaneous injections were given in amounts of 1 cc. daily for a period of 14 days prior to the administration of histamine.

Summary. The natural resistance of hypophysectomized rats treated with a crude emulsion of fresh anterior hypophysis during a period of 2 weeks following the operation to subsequent injections of histamine is increased almost to the normal level. The natural resistance of normal rats treated with a crude emulsion of fresh anterior hypophysis during a period of 2 weeks to subsequent injections of histamine is not appreciably increased.

8277 P

Effect of Vitamin A on Proliferation of Fibroblasts.

LILLIAN E. BAKER. (Introduced by T. M. Rivers.)

From the Laboratories of the Rockefeller Institute for Medical Research.

The purpose of the experiments reported here was to ascertain whether or not vitamin A is one of the substances needed by fibroblasts for their life and proliferation *in vitro*. Two previous investigators have already attempted to answer this question. Unfortunately, however, they arrived at opposite conclusions. Thus, Bur-