

## 7865 P

## Effect of Suprarenal Cortical Hormone on the Natural Resistance of Pituitarectomized Rats.

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We studied the effect of partial and complete pituitarectomy in rats on the natural resistance to histamine poisoning and correlated the anatomical changes in the suprarenal gland with the variations in resistance.<sup>1</sup> We noted that complete pituitarectomy in rats from 1 to 10 weeks after operation depressed the natural resistance of these animals to histamine poisoning. The M.L.D. was one-fifth to one-third that for normal rats. This decrease in resistance, we found, was associated with involutional changes of the suprarenal gland, such as hemorrhage into or atrophy of the inner zones of the cortex.<sup>2</sup> 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 natural resistance following pituitarectomy in the rat is probably secondary to the atrophic changes of the suprarenal cortex induced by the withdrawal of the adrenotropic hormone of the anterior lobe.\*

In the present studies the effect of the repeated injections of suprarenal cortical hormone, in pituitarectomized rats, on the natural resistance of these animals to histamine poisoning was observed.

Eighteen totally pituitarectomized adult albino rats were divided into 2 groups. Ten of these were given, during a period of 6 days, 2 injections daily of cortical hormone in amounts of 1 cc. per rat per day [equivalent to 40 gm. of fresh ox cortex (eschatin, Parke, Davis and Co.)] The interval between pituitarectomy and the day the treatments were begun varied from 5 to 8 days, but in one instance the rat had been pituitarectomized 89 days prior to the injections of the cortical hormone. Eight pituitarectomized rats received no cortical hormone injections. Those rats treated with

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<sup>1</sup> Perla, D., and Rosen, S. H., in press.

<sup>2</sup> Perla, D., *PROC. SOC. EXP. BIOL. AND MED.*, 1935, **32**, 655.

\* The literature on the evidence of the interrelationship of the anterior lobe of the pituitary and the suprarenal cortex is reviewed in an earlier paper<sup>2</sup> and by Shumacker and Firor.<sup>3</sup>

<sup>3</sup> Shumacker, H. B., and Firor, W. M., *Endocrin.*, 1934, **18**, 676.

TABLE I.  
Effect of Repeated Injections of Suprarenal Cortical Hormone on Natural Resistance of Pituitarectomized Adult Albino Rats to Histamine Poisoning.\*

Rat No.	Sex	Operat. Proced.	Days bet. Opera. and Injec. of Cortin		Days bet. Opera. and Injec. of Histam.	Wt. at Opera. gm.	Wt. of Cortical treatment gm.	Wt. time of Histamine injec. gm.	Amt. Hist. in mg. per Kg. body wt.	Result	Comment
			7	14							
1	M	C.P.						196	700	Survived	
2	F	"	6	14		205	183	180	800	"	
3	M	"	5	13		191	178	233	800	Died	
4	M	"	5	13		271	221	153	700	Survived	
5	M	"	8	14		144	140	145	700	Died	Survived 2 da. after hist. inj.
6	M	"	8	14		174	150	161	800	Survived	
7	F	"	7	12		154	132	130	800	"	
8	M	"	6	11		157	138	130	700	Died	Mkd. atrophy of supraren.
9	M	"	5	11		149	140	152	600	Survived	
10	M	"	89	95		167	145	154	800	Died	Extreme atrophy supraren.
Rats Treated with Cortin											
11	F	"	No Cortin	12		165	150	150	400	Died	
12	F	"	"	13		152	117	117	400	Survived	
13	M	"	"	54		205	170	170	700	Died	
14	F	"	"	50		191	170	170	600	"	
15	M	"	"	11		179	160	160	200	Survived	
16	F	"	"	12		152	124	124	200	Died	
17	F	"	"	15		161	140	140	300	"	
18	M	"	"	16		180	158	158	400	"	
19	M	O.C.	"	14		210	192	192	900	Survived	
20	F	"	"	12		212	196	196	600	"	
21	F	Normal	"	"		"	165	165	900	"	
22	M	"	"	"		"	185	185	900	Died	
23	F	"	"	"		"	160	160	1000	"	
24	M	"	"	"		"	190	190	1000	"	

\*All treated rats received 0.5 cc. of cortical hormone (equivalent to 40 gm. of whole cortex) twice daily over a period of 6 days prior to the injection of histamine.

Key to Chart: C.P. = Complete pituitarectomy. O.C. = Pituitary exposed but not removed.

cortical hormone were injected 6 days after treatment was begun with histamine in amounts ranging from 600 to 800 mg. of histamine per kg. of body weight (ergamine acid phosphate). Of 4 normal rats, 2 received 900 mg. of histamine per kg. and 2 received 100 mg. per kg. Two operated control rats received 600 and 900 mg. of histamine per kg. of body weight. The untreated pituitarectomized rats received histamine in amounts ranging from 200 to 700 mg. per kg. of body weight.

*Results.* The rats treated with cortical hormone appeared in most instances to be clinically improved and gained in weight, though no effect anatomically was observed on the degree of atrophy of the suprarenal cortex.†

Of the 10 pituitarectomized rats treated with cortical hormone the one receiving 600 mg. of histamine per kg. of body weight survived. Of 4 receiving 700 mg. per kg., 2 survived. Of 5 receiving 800 mg. per kg., 3 survived.

Of the 8 pituitarectomized rats not treated with cortical hormone and injected with histamine, of 2 rats receiving 200 mg. of histamine per kg. of body weight, one died; one receiving 300 mg. per kg., died; of 3 receiving 400 mg. per kg., 2 died; one receiving 600 mg. per kg. and one receiving 700 mg. per kg. died. The 2 operated controls (receiving no cortical hormone) survived 600 mg. and 900 mg. of histamine per kg. Of the normal controls the 2 receiving 1,000 mg. of histamine per kg. died; and of 2 receiving 900 mg. per kg., one died.

The repeated injections of large amounts of suprarenal cortical hormone raised the natural resistance of totally pituitarectomized adult rats to histamine poisoning. In some instances the resistance was raised almost to the level of normal rats. This is 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 pituitarectomized rats within 2 weeks after operation varies from 200 to 300 mg. per kg. of body weight.<sup>1</sup> Pituitarectomized 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.

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† Shumacker and Firor<sup>3</sup> mention that cortical hormone does not modify the anatomical changes of the suprarenal cortex induced by pituitarectomy. Kalk<sup>4</sup> treated a patient suffering with pituitary cachexia, with suprarenal cortical hormone and noted prompt improvement of the patient's condition. He believed that the pituitary cachexia is a result of the loss of suprarenal cortical function.

<sup>4</sup> Kalk, H., *Dtsch. Med. Wchnschr.*, 1934, **1**, 893.

These rats gained in weight in most instances and were apparently in better physical condition than untreated rats.

The effectiveness of the parenteral administration of any given amount of cortical hormone probably varies to some degree with the total cortical hormone which may be still available in the involuted suprarenal cortex.‡

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

### 7866 C

#### The Age Factor in Responsiveness to Gonadotropic Hormones.

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We reported<sup>1, 2</sup> that in very young rats (6-12 days old) A.P.L. (anterior pituitary-like hormone of pregnancy urine) leads only to the luteinization of theca cells but not to the formation of corpora lutea from granulosa cells. This theca-reaction is accompanied by continuous vaginal oestrus. This type of reaction to A.P.L. is very similar to that observed in hypophysectomized rats<sup>3</sup> and therefore the possibility of its being due to insufficient pituitary function at this early age had to be considered.

Corey<sup>4</sup> and Swezy and Evans<sup>5</sup> stated that pituitary implants have no effect on the ovaries of the rat during embryonic development, and during the first days of life. In order to see whether the effect of A.P.L. is different from that of the pituitary gonadotropic hormone during the first days of life, we repeated our earlier A.P.L.

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‡ It is of interest that in a pituitarectomized rat in which treatment was begun 95 days after operation, the rat gained in weight, but did not survive 800 mg. of histamine per kg. of body weight. Its suprarenals were found to be reduced to the size of a pinhead.

<sup>1</sup> Selye, H., Collip, J. B., and Thomson, D. L., *PROC. SOC. EXP. BIOL. AND MED.*, 1933, **30**, 647.

<sup>2</sup> Selye, H., Collip, J. B., and Thomson, D. L., *PROC. SOC. EXP. BIOL. AND MED.*, 1933, **30**, 780.

<sup>3</sup> Collip, J. B., Selye, H., and Thomson, D. L., *Nature*, 1933, **131**, 56.

<sup>4</sup> Corey, E. L., *PROC. SOC. EXP. BIOL. AND MED.*, 1928, **25**, 498.

<sup>5</sup> Swezy, O., and Evans, H. M., *Anat. Rec.*, 1931, **50**, 189.