

### Effect of Extract of Anterior Pituitary upon the Life-Span of Castrate-Adrenalectomized Cats.

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The writers have reported that a commercial extract of the anterior pituitary prolongs the life-span of bilaterally adrenalectomized cats, but is without effect upon dogs, at any rate in the dosage employed.<sup>1</sup> Two of the 12 animals studied were castrate males. One lived 25 days and succumbed to feline distemper; the other survived 47 days. It was deemed worth while to study the effect of A.P. extract upon the life-span of a larger group of castrate-adrenalectomized cats.

Strong, vigorous cats were used. They were given a vermifuge, and a few days later the gonads and right adrenal were removed under nembital anesthesia. They were then kept in the laboratory for 2 weeks to insure adjustment to laboratory conditions. The animal room was thermostatically regulated. The left adrenal was extirpated under ether and for 2 days following operation the cats received cortical hormone. If the animals were eating full rations at this time cortical hormone was withdrawn and A.P. extract substituted. The experiment began the day cortical hormone was discontinued.

The A.P. extract used was prepared by a modification of the method of Van Dyke and Wallen-Lawrence<sup>2</sup> and is an alkaline aqueous extract of cattle pituitary made by Squibb & Sons. It contains appreciable amounts of the various pituitary factors. We used freshly prepared non-preserved material since the cats appeared to be sensitive to the merthiolate present in the commercial preparation.

The diet consisted of 175 g of canned salmon plus 50 cc of milk daily. This was changed to fresh raw fish, liver and kidney whenever the appetite became capricious. The essential data regarding the effect of A.P. extract upon the life-span are shown in Table I.

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<sup>1</sup> Swingle, W. W., Parkins, W. M., Taylor, A. R., Hays, H. W., and Morrell, J. A., *Am. J. Physiol.*, 1937, **119**, 675.

<sup>2</sup> Van Dyke, H. B., and Wallen-Lawrence, Z., *J. Pharm. and Exp. Therap.*, 1930, **40**, 413.

TABLE I.  
Effect of A.P. Extract\* on Life-span of Castrate Bilaterally Adrenalectomized Cats.

Cat No.	Wt, kg	Sex	Survival period days	Cat No.	Wt, kg	Sex	Survival period days
1	4.02	♂	30	11	3.45	♂	11†
2	3.35	♂	23	12	3.45	♂	9
3	2.65	♂	15	13	2.25	♀	5 T
4	4.50	♂	14 T	14	3.43	♂	8 T
5	2.82	♀	15 T	15	3.26	♂	7†
6	3.80	♂	22	16	2.79	N.C. ♂	40
7	3.50	♂	28	17	2.58	N.C. ♂	49
8	3.10	♀	14	18	2.55	N.C. ♂	33
9	3.05	♂	31	S <sup>1</sup> 6	2.0	♂	25
10	3.48	♂	10	S <sup>1</sup> 10	2.10	♂	47

\*Daily dose = 1 cc/kg. N.C. = Non-castrate. S<sup>1</sup> = Castrates of earlier series. † = Sacrificed—respiratory infection. T = Terminal hypoglycemia.

Of a total of 17 castrate-adrenalectomized cats, 11 showed definite prolongation of the life-span and 6 did not. Several cases in the short-survival series were complicated by respiratory infections. The average life-span of the group (including 2 castrates of an earlier series<sup>1</sup>) was 18.4 days. The survival period ranged from 5-47 days. A group of 3 bilaterally adrenalectomized but non-castrate male cats were given daily injections of A.P. extract in comparable doses in order to compare the effect of the extract in animals with and without sex glands. The average life-span of this small group was 40.6 days. In the earlier work on the non-castrate male and female cat injected with A.P. extract a series consisting of 10 animals were studied.<sup>1</sup> One animal survived 150 days and died of adrenal insufficiency 4 days after the A.P. extract was discontinued. Excluding this individual (since the life-span was exceptionally prolonged), the average survival for the remaining 9 non-castrates was 24.8 days. However, if the 3 non-castrates of the present series are included with the non-castrates previously described (9 animals) the average survival of the 12 individuals on A.P. extract is 32.7 days. Thus it seems clear that the non-castrate A.P. injected adrenalectomized cats survive longer than similarly injected but castrated animals (av. 18.4 days). The sex of the animal does not appear to be important in so far as the effect of the A.P. extract is concerned.

Although the A.P. extract prolongs the life-span of both castrate and non-castrate cats it by no means substitutes for the adrenal cortical hormone. The animals (especially the castrates) soon become sluggish, vigor decreases, the hair becomes rough and shaggy and

tends to fall out, the appetite is capricious and all exhibit a slowly progressing cachexia. The long-surviving cats present a perfect picture of an animal suffering from chronic adrenal insufficiency. Terminal hypoglycemia is not uncommon in those individuals showing marked cachexia.

The explanation of the ameliorative effect of A.P. injections is not clear and this is especially true of the castrate animals. Since the A.P. extract contained some of the adrenotropic factor it is possible that microscopic cortical rests might have been stimulated sufficiently to elaborate enough of the vital hormone to maintain life. Although we have diligently searched for such accessories at autopsy none have been observed.

There can be no question but that the hormone of the corpus luteum ameliorates the symptoms of adrenal insufficiency in certain animals. This is well shown by the effects of pseudopregnancy upon the life-span of the adrenalectomized dog and ferret.<sup>1,3,4</sup> Collings<sup>5</sup> working in this laboratory has likewise demonstrated the striking effect of experimentally induced pseudopregnancy upon the life-span of the adrenalectomized cat.

Steiger and Reichstein<sup>6</sup> report that 21-oxy-progesterone has definite cortical hormone activity on adrenalectomized dogs and rats. The close similarity between progesterone and corticosterone<sup>6</sup> and the fact that 21-oxy-progesterone prolongs the life-span of adrenalectomized animals, apparently offers an adequate explanation for the effect of pseudopregnancy (which represents the corpus luteum phase of the cycle) upon the survival of the adrenalectomized dog, ferret and cat. Apparently the organism lacking adrenals has the ability to convert progesterone into corticosterone or related substances.

However, this does not explain the effect of A.P. extracts upon the life-span of the adrenalectomized male cat but suggestive evidence does exist. Thus Callow and Parkes<sup>7</sup> demonstrated the presence of appreciable quantities of progesterone in the testes of mammals. According to them, bull testes contain the equivalent of 1 mg of progesterone per 1400 g of tissue. It seems not unreasonable to assume that the testis of cats likewise contains progesterone and the daily injection of A.P. extract may stimulate the gonads to produce

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<sup>3</sup> Rogoff, J. M., and Stewart, G. N., *Am. J. Physiol.*, 1928, **86**, 20.

<sup>4</sup> Gaunt, R., and Hays, H. W., *Anat. Rec. (Suppl.)*, 1938, **70**, 29.

<sup>5</sup> Collings, W. D., unpublished work.

<sup>6</sup> Steiger, M., and Reichstein, T., *Nature*, 1937, **139**, 925.

<sup>7</sup> Callow, R. K., and Parkes, A. S., *J. Physiol. (Proceedings)*, 1936, **87**, 16.

excessive amounts which in time would be converted into corticosterone or related substances having cortical hormone-like activity. The fact that the A.P. injected non-castrate adrenalectomized cat is easier to maintain and survives longer than the similarly treated castrate fits well with this viewpoint. But the fact that the castrates also react to A.P. injections offers difficulties, unless it be assumed that other tissues besides the gonads can also form progesterone or related substances as a result of A.P. treatment.

Although the writers believe that the various factors enumerated may and probably do enter into the explanation of the ameliorative effect of A.P. extract on adrenal insufficiency in the cat, there remains another factor which we regard as important. This is the effect of A.P. extract upon the appetite, ingestion and digestion of foodstuffs, and the absorption and utilization of carbohydrate in these animals.

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#### **Influence of Posture on Skin and Subcutaneous Temperatures.**

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Previous experiments<sup>1</sup> showed that the cardiac output in the sitting and standing positions was less than in the recumbent. They also indicated the probability that the former positions facilitate the return of a disproportionately large amount of blood from the short systemic circuits, although the amount from the extremities and the splanchnic area is decreased. The present report deals with observations on blood flow, particularly in the extremities, as measured by surface and subcutaneous temperatures.

Eight adult subjects with normal cardiovascular systems have been systematically studied. Temperatures in various parts of the body were determined by means of surface and non-conducting hypodermic thermocouples in a potentiometric circuit so arranged as to permit rapid and accurate consecutive readings.<sup>2</sup> The subcutaneous thermocouples were inserted to a depth of from 2 to 4 mm. Passive

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<sup>1</sup> Sweeney, H. M., and Mayerson, H. S., *Am. J. Physiol.*, 1937, **120**, 329.

<sup>2</sup> Foster, P. C., *J. Lab. and Clin. Med.*, 1936, **22**, 68.