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Presence of Antithyrotropic Substance in Serum of Rats Injected Chronically with Rat Pituitary Extract.*

EVELYN ANDERSON AND HERBERT M. EVANS.

From the Institute of Experimental Biology, University of California, Berkeley.

It was reported by Katzman, Wade and Doisy[1] that female rats receiving chronic implantation of anterior lobes of the same species for as long as 9 months still possessed enlarged ovaries and that there was no evidence of the existence of gonadotropic- or thyrotropic-inhibitory substances in the plasma of these rats.

We have carried out an investigation with regard to the thyrotropic hormone which sufficiently parallels the method used by these workers so that we feel a comparison of results is justifiable. A group of rats were injected daily with an alkaline extract of rat anterior pituitary for periods of 18 to 122 days. Each rat received the equivalent of 1 or 2 adult pituitaries daily. The serum was collected from these animals at the time of autopsy. This was examined for antithyrotropic substance, using immature guinea pigs as the test animal. The animals were given 1 or 2 cc of serum daily for 4 days. On the second, third and fourth days, a standard alkaline extract of beef pituitary was injected, the total dose for the 3 days being equivalent to 6 adult rat pituitaries, which was the amount used by the workers referred to above. The O_2 consumption of the guinea pigs was measured daily during the 5-day test period. The animals were autopsied on the fifth day, which was 96 hours after the first injection of pituitary extract. The failure of the rise in O_2 consumption of test animals to the expected level with a standard dose of thyrotropic hormone when serum was given, has been taken as an indication of antithyrotropic activity of the serum. Our results are shown in Table I. It was found that 4 cc of rat serum had very little effect in preventing the rise in O_2 consumption, while 8 cc of serum caused a significant depression of the O_2 consumption. The St. Louis investigators did not use a dose of serum greater than 4 cc. This may explain their failure to obtain evidence of antithyrotropic activity.

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1 Katzman, P. A., Wade, N. J., and Doisy, E. A., *Endocrinology*, 1937, **21**, 1.

TABLE I.
Inhibitory Effect of the Serum from Rats Injected Chronically with Rat Anterior Pituitary Extract Using O_2 Consumption in Guinea Pigs as the Test Method.

	No. of days donors injected	Donors' serum total dose cc	No. of test animals	% change in O_2 consumption
1. Standard dose thyrotropic hormone only			25	+25
2. Normal rat serum	—	8	10	+20
3. Serum from rats injected with rat pituitary extract	18	4	2	+24
4. Serum from rats injected with rat pituitary extract	35	4	4	+23
5. Serum from rats injected with rat pituitary extract	35	8	6	+10
6. Serum from rats injected with rat pituitary extract	39	8	1	+14
7. Serum from rats injected with rat pituitary extract	122	4	4	+18
8. Serum from rats injected with rat pituitary extract	122	8	2	+ 9
9. Serum from rats injected with beef pituitary extracts*	120	4	13	— 2

The test guinea pigs received a total dose of standardized extract of beef pituitary which was equivalent to 6 adult rat pituitaries in terms of thyrotropic activity.

*The donors in this series were injected with an alkaline extract of beef anterior pituitary. The daily dose had 10 times the thyrotropic activity of one adult rat pituitary.

It may well be that if larger doses of thyrotropic hormone from rat pituitaries had been injected over a prolonged period, a serum more potent in antithyrotropic activity would have been obtained. We have included in Table I the effect of serum from rats which had been injected with beef pituitary extracts for 120 days, receiving a daily dose of thyrotropic hormone equivalent to 10 rat pituitaries, which was 5 to 10 times the dose given the rats in the other series. Four cc of this serum completely inhibited the effect of the standard test dose of thyrotropic hormone.

Conclusion. The injection of rat pituitary extract into rats gives rise to an antithyrotropic substance in the serum of these animals. This was detected by the depressing effect of the serum upon the O_2 consumption of guinea pigs receiving a standard dose of thyrotropic hormone.