NDV-induced toxic corneal reactions. In most animals this treatment suppressed development of opacity and reduced markedly the extent of fusions of endothelial cells. It did not inhibit formation of endothelial rosettes. The suppressive effects in the HN_2-treated animals lasted for at least 20 days, well after leucopenia had disappeared. Decreased response to injected virus is neither a result of suppression of circulating leucocytes nor of rapid inactivation of virus in aqueous humor.

Treatment of rabbits with a single intravenous injection of HN_2 4 days, 2 days, or immediately before virus injection caused no demonstrable suppression of virus-induced toxic reactions of rabbit corneas. Leucocytes appeared to play no essential role in production of corneal reaction.

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Correlation of Pituitary Ribonucleic Acid Levels and ACTH Production Following Adrenalectomy and Cortisone Administration.* (26357)

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It has been inferred that withdrawal of adrenal cortcial hormones enhances both release and synthesis of pituitary adrenocorticotrophic hormone (ACTH), but with a predominent effect on synthesis. The latter mechanism serves to explain the increased concentration of ACTH in pituitary tissue following adrenalectomy(1,2,3). The inhibitory effect of adrenal cortical hormones on ACTH content of pituitaries and plasma likewise has been attributed to alteration of rates of trophic hormone production and release (3,4).

Since the relationship of ribonucleic acid (RNA) and protein synthesis has been shown to be applicable to pituitary hormone production following adrenalectomy(5), one can correlate fluctuations in tissue content of ACTH following adrenalectomy and cortical hormone administration, as demonstrated by Fortier(1,4), with RNA levels in the hypophysis. This report, based on pituitary RNA content following adrenalectomy or adrenal cortical hormone treatment, is an attempt to correlate protein synthetic activity with conent of trophic hormone in the tissue.

Methods. Male rats of the Holtzman strain were bilaterally adrenalectomized *via* dorsal approach and maintained on Purina Laboratory Chow pellets and 1% NaCl *ad lib*. Unoperated rats of the same age, receiving tap water in place of salt solution, served as controls. At intervals of time from ½ hour to daily and weekly post-operative periods (Table I), adrenalectomized and control rats were sacrificed. Other rats received

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TABLE I. Effect of Adrenalectomy on Pituitary RNA.

Post-operative time	μg RNA/mg tissue	Post-operative time	μg RNA/mg tissue
Control	7.5 ± .3*(33)		
½ hr	9.9† ± .2 (6)	30 hr	7.9 ± .2 (15)
1 "	8.4 ± .1 (6)	48 "	12.6† ± .5 (9)
2 "	7.6 ± .4 (6)	7 days	8.0 ± .3 (12)
3 "	8.0 ± .1 (6)	14 "	9.5† ± .2 (15)
6 "	8.7 ± .2 (9)	21 "	8.4 ± .5 (18)
12 "	7.0 ± .3 (24)	32 "	9.4† ± .5 (6)
24 "	6.9 ± .3 (12)		

* Stand. error.
† Difference from controls statistically significant.
No. of animals in parentheses.

Cortone Acetate (Cortisone Acetate, Merck), 6 mg/100 g I.P., or an equal volume of saline daily for 4 weeks. At time of sacrifice, rats were decapitated, anterior pituitary tissue collected, weighed and assayed for RNA content as previously reported(6).

Results. During the first 30 hours following adrenalectomy, the only significant rise in pituitary RNA over control levels, of various time periods studied, occurred in those rats sacrificed at ½ hour post-operatively. A rise of 32% decreased to values not significantly different from controls at one, 2, 3 and 6-hour intervals (Table I). Concentration of pituitary RNA at 12 and 24-hour post-operative periods was somewhat below that of controls, but returned to a normal level 6 hours later (Table I). The most marked increase in RNA concentration, a 68% rise, occurred in those rats adrenalectomized for 48 hours. Pituitary RNA of rats operated for 7, 14, 21 and 32 days fluctuated from normal to elevated levels rhythmically (Table I).

The dosage of cortisone utilized produced marked reduction in body and adrenal weights of treated animals compared to controls. The treatment also resulted in a 21% reduction in concentration of pituitary RNA (Table II).

Discussion. Plotting pituitary RNA in μg/mg tissue against time after adrenalectomy, the curve in Fig. 1 is obtained. Comparison of this curve with that depicted for pituitary ACTH concentration after adrenalectomy(1) shows remarkable similarity up to 2 post-operative days. The rise in pituitary RNA ½ hour post-operatively coincides with elevated tissue content of ACTH at that time. Furthermore, the fall in ACTH

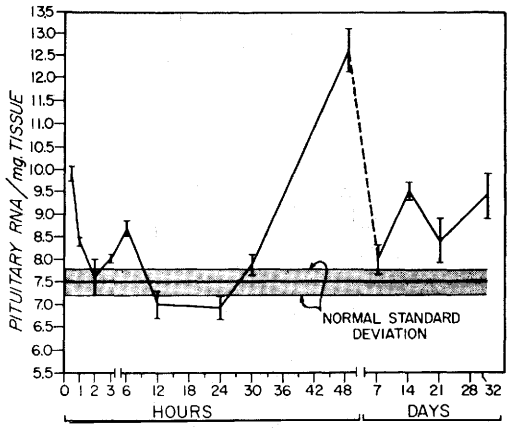

FIG. 1. Effect of bilateral adrenalectomy on pituitary RNA concentration (in μg/mg tissue) in relation to time (hr and days). Shaded area indicates control value with stand. error (S.E.). Lines above and below each of the points on the curve indicate S.E.'s.

concentration to below control levels during the next 24 hours is reflected in the pituitary RNA by a return to normal at 6 hours and subnormal levels at 12 and 24 hours post-adrenalectomy. The second rise in pituitary ACTH begins between the first and fourth post-operative day in Fortier's curve(1), which once again coincides with the rise in pituitary RNA 48 hours after surgery. How-

TABLE II. Effect of Cortisone on Pituitary RNA.

Group	Body wt (g)	Rel. adr. wt (mg/100 g B.W.)	Pit. RNA (μg/mg tissue)
Controls (20)—.2 cc saline/100 g/day	259 ± 5*	12.7 ± .3*	8.0 ± .2*
Treated (19)—6 mg cortisone/100 g/day	170† ± 6	7.9† ± .4	6.3† ± .2

* Stand. error.
† Difference from controls statistically significant ($p < .001$).
No. of animals in parentheses.

ever, continued increase in hormone concentration in the tissue is not reflected in sustained high levels of pituitary RNA.

The polyphasic response of pituitary ACTH to adrenalectomy can be explained in relation to protein synthetic activity taking place in the tissue as measured by RNA content. The initial rise in RNA ½ hour postoperatively, indicating accelerated rate of synthesis, accounts for increased tissue content of ACTH. The subsequent decrease in tissue content of ACTH, reflecting predominance of hormone release over synthesis(1), is revealed by the diminished RNA values from one to 30 hours after surgery.

The secondary rise in ACTH content is preceded by markedly accelerated rates of protein synthesis as evidenced by high levels of pituitary RNA. The fact that the tissue continues to accumulate increased amounts of ACTH without accompanying indices of accelerated synthesis may be explained by one or both of the following hypotheses. It may be that once initiated (48 hours postadrenalectomy), the pituitary gland can produce increased amounts of ACTH without an exaggerated rate of protein synthesis. Or it may be that the accumulation of endogenous ACTH in the tissue exerts a depressing effect on the synthetic processes comparable to the observation made by Gemzell and Heijkenskjöld utilizing exogenous ACTH to suppress pituitary content of the hormone in adrenalectomized animals(7).

The depressing effects of adrenal cortical steroids on pituitary ACTH content(3,4) are likewise reflected in the RNA picture. If cortical hormones act to inhibit ACTH synthesis, as suggested by Hodges and Vernikos (3) and Fortier(4), the low level of tissue RNA following cortisone treatment adds further support to the pituitary protein synthetic inhibition produced by adrenal steroids.

That the tissue content of RNA is associated with protein synthetic activity and not hormone release is based on the following observations. Although pituitary RNA and ACTH levels are high within a few days following adrenalectomy, circulating adrenocorticotrophin cannot be easily detected until 3-5 weeks after surgery(8). In cortisone-treated rats, the small adrenal weights together with reduced pituitary RNA and ACTH contents may indicate inhibition of both synthesis and release of trophic hormone. However, the failure to completely prevent the rise in blood corticotrophin of stressed-adrenalectomized rats with adrenal steroid(3) indicates the action of cortical hormone is not on release.

Summary. The concentration of RNA in pituitary tissue was determined following various periods of adrenalectomy and prolonged cortisone treatment. Elevations of pituitary RNA at ½ and 48 hours post-operatively correlate with increased tissue content of ACTH reported for the post-adrenalectomy periods. Reduction in level of tissue RNA following cortisone administration likewise correlates with decreased amounts of ACTH in pituitaries reported after such treatment. The data, utilizing tissue RNA as an index of protein hormone synthetic activity, provide further information that indicate adrenal cortical steroids regulate synthesis of ACTH.

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