show a transformation of cortisone to 17-ketosteroids that is much greater than normal, while the base-line excretion tends to be in the low-normal or below-normal range. The latter finding is in accord with the observations of Miller and Mason (*15*) and Lundbaeck (*16*). At the same time, base-line levels of corticosteroid excretion, although variable, tend to lie within the normal range (*17*).

The present findings suggest a possible altered steroid metabolism in diabetes mellitus. Their significance may be clarified by studies now in progress. A more detailed report of this study will be submitted for publication elsewhere.

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Effect of Reserpine on Adrenocortical Function in Unanesthetized Dogs

Reserpine produces tranquility in agitated patients (*1*), and depressed hypothalamic function has been suggested as the mechanism of this action. Because the hypothalamus is involved in the regulation of ACTH secretion from the adenohypophysis (*2*), an assessment of adrenocortical function following reserpine administration is indicated. Gaunt and coworkers (*3*) have demonstrated adrenocortical hypertrophy in rats following reserpine administration—a finding suggesting stimulation of ACTH secretion rather than suppression. The present study (*4*) was undertaken to determine the effect of reserpine on adrenocortical function in dogs; we employed a direct and specific method for evaluating the secretory activity of the adrenal cortex.

Table 1. Effect of intravenous reserpine on adrenal 17-hydroxycorticosteroid secretion in unanesthetized dogs. Output values for right adrenal gland only. When zero output is indicated, steroid concentration was below the sensitivity of the analytic method (0.1 to 0.2 μg).

Dog No.	Dose of reserpine		Minutes prior to injection			Adrenal 17-hydroxycorticosteroid output (μg/min) Minutes after injection								
	mg	mg/kg	10–20	5–10	0–5	0–5	5–10	10–20	20–30	30–45	45–60	60–90	90–120	120–180
1	5	0.12	1.3	0.4	0.5	1.0	0.0	0.0	1.3	17.5				
2	5	0.18		0.0	0.0	0.0	0.0	0.0	0.0	0.4	15.5			27.4
3	5	0.21	0.0		0.0	0.0	0.0	0.0	0.0	5.2	20.0	2.6	18.1	29.4
4	5	0.31	0.0	0.2	0.1	0.1		1.6	19.0	17.8	6.4	13.0		15.4
5	5	0.33	1.1	0.5	0.8	0.4	7.8	12.2	8.5		15.1	24.7	12.0	

In each of five male mongrel dogs, the right lumboadrenal vein was cannulated according to a technique described by Hume and Nelson (*5*). After a recovery period of 48 hours, samples of adrenal venous blood were collected from the resting, unanesthetized animals. Each dog was then given 5 mg of reserpine (Serpasil, Ciba) intravenously, and samples of adrenal venous blood were collected at intervals thereafter. All blood samples were analyzed for 17-hydroxycorticosteroid content (*6*). The animals became drowsy soon after the reserpine injection and remained so during the 3-hour period of blood sampling.

The results are presented in Table 1. Following reserpine administration, a marked increase in adrenal corticoid secretion was observed in all cases. In four dogs, the response was delayed, with highest values occurring between ½ and 3 hours after drug injection. The maximal corticoid values following reserpine administration are similar in magnitude to those obtained following the intravenous injection of large doses of ACTH, though comparatively much delayed. While it may be assumed that the increase in adrenal steroid secretion following reserpine injection is mediated by ACTH secreted from the adenohypophysis, the mechanism underlying the delay in response remains obscure. This study indicates that reserpine, in the doses used, is a potent stimulus to adrenal cortical secretion in unanesthetized dogs. It should be emphasized that these results represent an acute response to a large dose of reserpine. They do not necessarily imply that any comparable adrenal response occurs to smaller oral doses used in clinical practice.

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Note on Murphy's and Rhine's Comments

In recent issues of *Science* there have appeared comments by Murphy (*1*) and by Rhine (*2*), criticizing our report of "A methodological refinement in the study of 'ESP,' and negative findings" (*3*). We feel that these comments call for a brief rejoinder.

Both Murphy and Rhine seem inclined to dismiss our findings on the basis of the fact that our study "did not even pretend to replicate any previous research" (*2*) in the field of extrasensory perception. We can but point out that methodological improvement is generally considered a scientific desideratum and that the comparison of results obtained by one methodology with those obtained by another is a common scientific procedure.

Both critics object, also, to the nature of the targets employed in our study. In an effort to forestall such objections, we communicated in some detail with Rhine, as he has stated (*2*), before we actually undertook our experiment. We were particularly concerned with the question of the form of the targets and called it especially to Rhine's attention. Rhine's only misgivings on this point had to do with the issue of the "stacking error" (*2*; compare with Rhine, *4*), an issue that happens to have no relevance for our experimental design. Although he now makes an assertion to the contrary (*2*), Rhine did not at that time object to "the curious device of making