In patients with interval gout or a uric acid diathesis severe acute attacks may appear for the first time following the withdrawal of ACTH and cortisone. This may be treated by either reinstituting ACTH and cortisone treatment for an additional 24-48 hours together with colchicine or using colchicine alone.

Hormonal Changes.—Functional Depression of the Pituitary-Adrenocortical Axis: Evidence has been obtained from several sources that following the withdrawal of cortisone there is a temporary functional depression of the adrenal cortex.[3] It is characterized by asthenia and lassitude. The presence of adrenal insufficiency may be shown by a failure of the adrenal cortex to respond to ACTH stimulation. This unresponsiveness usually lasts four to seven days, but on occasion in patients who have had prolonged courses of cortisone therapy the adrenal cortical depression may last as long as 10 to 14 days (table 3). If the development of adrenal cortical insufficiency is acute, it may prove fatal. Therefore, it is important with cortisone or with other types of adrenal steroid therapy, such as 17-hydroxycorticosterone (compound F), to reduce the dose gradually and slowly increase the interval between doses before the complete cessation of treatment. It may also be prevented by administering ACTH during the withdrawal of cortisone. This allows the depression of the anterior pituitary adrenocorticotropic mechanism to disappear gradually and leads to increasing amounts of endogenous corticotropin production, stimulation of the patient's adrenal cortices and eventually restoration of the pituitary adrenocortical system to normal.

TABLE 3.—*Adrenal Cortical Depression During Cortisone Treatment in a Woman Aged 35 with Hyperthyroidism*

Treatment	17-Ketosteroids (Mg./24 Hr.)*	4-Hr. ACTH Test Fall in Eosinophils, Per Cent
0	8.8	—96%
Cortisone, 100 mg. × 10 days	4.6	.....
Cortisone, 200 mg. × 6 days	7.6	.....
0 × 6 days ACTH, 40 mg. × 2 days	7.6	— 7%

* Cortisone therapy has caused a reduction in 17-ketosteroids excretion. This suppression of adrenal cortical activity is also shown by the failure of ACTH to cause a rise in 17-ketosteroids or a significant fall in circulating eosinophils.

Following the administration of ACTH there is also functional depression of the adrenal cortex, and temporary adrenal insufficiency develops. It is due to suppression of endogenous pituitary production of corticotropin, is less prolonged and less complete than that following cortisone, since the adrenal itself remains enlarged, capable of active secretion and in a state of ready responsiveness to stimulation. The development of adrenal cortical insufficiency is readily prevented if the ACTH is gradually reduced before it is discontinued. Epinephrine has been suggested as a possible means of stimulating the functionally depressed pituitary but has not proved effective in this regard.

3. Sprague, R. G.; Power, M. H.; Mason, H. R.; Albert, A.; Mathieson, D. B.; Hench, P. S.; Kendall, E. C.; Slocumb, C. H., and Polley, H. F.: Observations on the Physiological Effects of Cortisone and ACTH in Man, Arch. Int. Med. **85**:199-258 (Feb.) 1950. Forsham, P. H.; Thorn, G. W.; Frawley, T. F., and Wilson, D. L.: Studies on the Functional State of the Adrenal Cortex During and Following ACTH and Cortisone Therapy, J. Clin. Invest. **29**:812, 1950. Thorn and others.[1c]