close relationship between mineralocorticoid and prophlogistic (anticortisol) potency. They demonstrate furthermore, by comparison with our earlier findings concerning aldosterone(2), that Me-F-COL—a synthetic steroid not known to occur in nature—at least equals, and probably exceeds, the anticortisol activity of the most potent natural mineralocorticoid.

Summary. In adrenalectomized rats bearing a "granuloma pouch," it has been demonstrated that 10 μg/day of 2-methyl-9(α)-fluorocortisol (Me-F-COL) definitely antagonizes the catabolic, antiphlogistic, thymolytic and splenic atrophy-producing actions of 400 μg/day of cortisol acetate (COLA). Higher doses of Me-F-COL are less effective in these respects. Since Me-F-COL possesses some glucocorticoid potency, in addition to its strong mineralocorticoid effect, the comparatively low anticortisol activity of this compound, when it is given at high dose-levels, is in agreement with expectations based on the "law of intersecting dose-effect curves."

Addendum. Since this manuscript went to press we were able to show that Me-F-COL is more than 100 times as active as DOCA in producing nephrosclerosis and cardiovascular hyalinosis in suitably conditioned rats (Selye, H., and Bois, P., *Endocrinology,* in press).

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Diffusion Coefficient of Urate for Human Connective Tissue Membrane. (22479)

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Determinations of the diffusion coefficient of urate for connective tissue have not as yet been reported. The present study was carried out on 10 samples of the cerebellar tentorium, obtained fresh at autopsy, using the diffusion method of Johnsen and Kirk(1). In this procedure the diffusion rate of a compound from one fluid phase to another through a membrane is measured under sterile conditions and at a constant total pressure.

Methods. The experiments were conducted at 37°C. A solution of sodium urate (190-197 mg %) in Krebs' phosphate buffer, pH 7.4, was used in the donor compartment of the apparatus, and phosphate buffer in the recipient compartment. The urate solution was prepared fresh daily by addition of 20 ml 0.1 N NaOH solution to 200 mg of uric acid contained in a beaker. The beaker was placed in a water bath at 60°C, and the solution stirred vigorously. 60 ml of Krebs' phosphate buffer, preheated to 60°C, were then added; after adjustment to pH 7.4 the solution was made up to 100 ml with phosphate buffer, and, after cooling to 25°C, was filtered through a Whatman No. 2 filter paper. The purpose of the cooling and subsequent filtration was to insure against precipitation of urate from the solution during the experiment. For the diffusion experiment the tentorium sample was rinsed with sterile buffer solution and a portion of the membrane inserted in the diffusion apparatus. Both the donor and recipient solutions were heated to 37°C before they were introduced into the apparatus. 45 minutes were allowed to elapse for establishment of temperature equilibrium and for initial penetration of urate through the membrane before the first samples were withdrawn for analysis. In each experiment 2 diffusion periods of 90

minutes were used. The sample withdrawals were carried out in immediate succession from the donor and recipient compartments at the beginning and end of a diffusion period; this made it possible to employ the equation given by Pletscher *et al.*(2) for calculation of the diffusion coefficient. The diffusion coefficient is defined according to Hill(3) as the number of units of the compound diffusing through a 1 cm^2 area of the membrane in 1 minute at a concentration gradient of 1 unit per ml per cm.

The determination of the urate content of the samples was performed by enzymatic differential spectrophotometry(4), using a Beckman DU spectrophotometer. To prevent precipitation of urate through cooling the collection of the samples from the diffusion apparatus was made in test tubes heated in a water bath to 50°C. Before analysis the samples from the donor compartment were diluted with glycine buffer in the proportion of 1:250, whereas dilutions of 1:2.5, 1:10, and 1:25 were employed for the first, second, and third samples, respectively, from the recipient side. The dilutions were carried out in such a way that a final glycine concentration of 0.067 M was obtained. At the end of the experiment the part of the membrane which had been delimited by the circular openings of the metal diaphragms of the apparatus was carefully cut out and its area and weight were determined. From these values the mean thickness of the membrane was calculated.

Results. The results of the diffusion coefficient determinations are presented in Table I. The average urate diffusion coefficient value found was 0.000155 ± 0.000011.

TABLE I. Diffusion Coefficient of Urate for Human Cerebellar Tentorium.

Sex	Age (yr)	Thickness of tentorium (mm)	Diffusion coefficient of urate 1st period	2nd period	Avg
♂	24	.518	.000111	.000119	.000115
♀	24	.568	.000131	.000116	.000123
♂	31	.483	.000157	.000150	.000154
♂	37	.517	.000183	.000197	.000190
♀	50	.480	.000149	.000138	.000145
♂	55	.521	.000168	.000174	.000171
♂	55	.310	.000124	.000133	.000129
♂	56	.683	.000210	.000256	.000233
♀	57	.697	.000176	.000140	.000158
♂	67	.648	.000137	.000124	.000131
		Mean	.000155	.000155	.000155

No significant correlation was noted between the age of the individuals from whom the connective tissue membranes were derived and the coefficient values measured.

Summary. Determinations were made at 37°C by the method of Johnsen and Kirk of the diffusion coefficient of urate for a human connective tissue membrane (cerebellar tentorium). The urate analyses were performed by enzymatic differential spectrophotometry. The average coefficient value found in experiments on 10 samples was 0.000155.

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