(0.013), *E* (0.05), *F* (0.14), and *G* (0.12). A visible absorption curve (400–800 mμ) of the blue reaction product that was formed from *C–G* was identical with that of authentic lysergic acid. Pharmacological assays by C. E. Powell (*5*) demonstrated an ergonovine type of activity in extracts of samples *C* to *G*. Papergrams in a butanol-acetic-water system (*6*) identified ergonovine as the major component in the extracts exhibiting a blue fluorescence under ultraviolet light.

From these results it is apparent that the ergot alkaloids are largely synthesized in the fungus during the later stages of sclerotial development. No lysergic acid could be detected in samples *A* and *B* before pigment and sclerotium formation. Traces of the alkaloids appeared 12 days after inoculation. The amount gradually increased to a maximum on the 19th day when the fungus was still increasing in weight.

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Anticortisol Action of Aldosterone

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Since the first description of the general-adaptation syndrome as the body's standard response to stress, much attention has been given to the role played by adrenocortical hormones in the pathogenesis of various diseases. There is no longer any doubt that an increase in the secretion of ACTH and glucocorticoids (for example, cortisol) is an essential prerequisite for the maintenance of homeostasis during stress. It has also been shown that many activities of these hormones are inhibited by simultaneous treatment with somatotrophin or mineralocorticoids (for example, desoxycorticosterone). The medical importance of a proper balance between gluco- and mineralocorticoids is most evident with regard to inflammation, because, in general, glucocorticoids suppress, while mineralocorticoids enhance, inflammatory responses to tissue injury. Consequently the former hormones have also been referred to as "antiphlogistic" and the latter as "prophlogistic" corticoids (*1–3*).

The greatest weakness of this theory was the lack of any direct proof that the adrenal gland actually secretes physiologically effective quantities of a mineralocorticoid comparable to desoxycorticosterone. This gap in our knowledge has now been filled by the discovery of "aldosterone," a highly active natural mineralocorticoid (*4*). Yet, the question still remained whether aldosterone is actually an antagonist of glucocorticoids.

Ninety-six female Sprague-Dawley rats, weighing 151 to 170 g (average 160 g), were bilaterally adrenalectomized and subdivided into four groups, as is indicated in Table 1. Throughout the observation period these rats were maintained exclusively on Purina Fox Chow and tap water, without special salt supplements.

Hormone treatment was initiated on the day of adrenalectomy. Cortisol was given in the form of Hydrocortone Acetate microcrystals (Merck) at the daily dose of 400 μg in 0.2 ml of aqueous suspension medium, subcutaneously in the chest region. Aldo-

Table 1. Anticortisol action of 20 μg/day of aldosterone in adrenalectomized rats.

Group	No. of rats	Treatment	Final body weight (g)	Weight gain (g)	Exudate (ml)	Thymus (mg)	Spleen (mg)	Mortality (%)
I	40	None	178 ± 7.3	+18	14 ± 3	603 ± 41	966 ± 206	87
II	40	Cortisol	132 ± 3.6	−28	3 ± 0.9	69 ± 8.3	490 ± 23	5
III	6	Aldosterone	172 ± 7	+12	12 ± 2.7	369 ± 46	934 ± 79	50
IV	10	Cortisol and aldosterone	155 ± 5.5	− 5	10 ± 1.2	105 ± 11	814 ± 113	0

Table 2. Anticortisol action of 50 μg/day of aldosterone in adrenalectomized rats.

Group	No. of rats	Treatment	Final body weight (g)	Weight gain (g)	Exudate (ml)	Thymus (mg)	Spleen (mg)	Mortality (%)
I	8	Cortisol	141 ± 5.6	−19	8 ± 1.6	146 ± 13.9	665 ± 48.3	0
II	9	Cortisol and cholesterol	137 ± 3.6	−23	9 ± 2.3	138 ± 22.8	690 ± 75.6	0
III	6	Cortisol and aldosterone	161 ± 3.3	+ 1	17 ± 1.0	191 ± 16.0	959 ± 98.3	0
IV	10	Cortisol and DCA	158 ± 2.1	− 2	13 ± 2.1	229 ± 18.0	978 ± 69.9	0

sterone (Ciba) (*5*) was injected into the inguinal region, at the dose of 20 μg/day in 0.2 ml of sesame oil.

For the quantitative assessment of inflammation, "granuloma-pouches" (*6*) were prepared 48 hr later by the injection of 25 ml of air under the dorsal skin; this was immediately followed by the injection of 0.5 ml of 1-percent croton oil (in corn oil) into the air space so created. All the animals were killed on the 14th day after adrenalectomy.

It is evident from Table 1 that, under these conditions, 20 μg of aldosterone slightly but significantly diminished the body-weight loss ($P < 0.01$) and the inhibition of inflammatory-exudate formation ($P < 0.01$) by cortisol. However, the involution of the thymus and spleen was not significantly suppressed.

A second experiment was therefore performed with a higher daily dose of aldosterone, but, in view of the scarcity of this hormone, the length of treatment had to be shortened. Thirty-six female Sprague-Dawley rats, weighing 154 to 163 g (average 160 g), were treated in essentially the same way as those of the first experiment, except that the granuloma-pouch was prepared on the first day, while treatment with steroids was begun 48 hr later, simultaneously with bilateral adrenalectomy. The dose of aldosterone was raised to 25 μg twice daily in 0.25 ml of sesame oil, and we added additional controls to which cholesterol (as an inactive steroid) and desoxycorticosterone acetate (Schering) (DCA, as a proved prophlogistic corticoid) were administered at the same dose level. For uniformity's sake, cortisol was also given in two daily subcutaneous injections (each 200 μg in 0.25 ml of water). The animals were killed on the 12th day.

Table 2 indicates that, at the dose level of 50 μg/day, aldosterone inhibits a variety of characteristic cortisol actions. In this respect it is approximately equally active as DCA. Cholesterol—a hormonally inert compound—is devoid of such an inhibitory action.

Depending upon the test used, the mineralocorticoid activity of aldosterone has variously been estimated to be about 25 to 125 times that of desoxycorticosterone (*7*). On the other hand, with regard to their anticortisol effects, we find no striking quantitative difference between the activities of the two steroids. It is noteworthy, however, that despite this the natural mineralocorticoid, aldosterone, inhibits all the afore-mentioned morphologic actions of the natural glucocorticoid, cortisol in the proportion 1:8.

Thus, the concept according to which a balance between two opposing naturally secreted corticoids can regulate the course of various biologic phenomena, including inflammation, has now been proved by direct experimental observations, using corticoids the presence of which in the circulating blood had been demonstrated beyond doubt (*8*).

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Gramine Derivatives Antagonistic to 5-Hydroxytryptamine (Enteramine)

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It has been previously demonstrated that gramine (3-dimethylaminomethylindole) possesses, both *in vitro* and, to a lesser degree, *in vivo* a clear action antagonistic to 5-hydroxytryptamine (5-HT) (*1, 2*). In the present paper are briefly reported the main results obtained with nine gramine derivatives synthesized by Colò *et al.* (*3*) in the Farmitalia Research Laboratories.

The anti-5-HT activity of these derivatives was studied in respect to the spasmogenic effect of 5-HT on the rat estrous-uterus and to the antidiuretic effect of the substance in hydrated rats (*4*).

Table 1 shows the approximate dose of antimetabolite necessary to halve the uterus-stimulant effect produced by 0.1 μg of 5-HT base. For comparative purposes the values obtained with three of the most representative aminoindoles of Woolley and Shaw (*5*) are also included in the table: 2-methyl-3-ethyl-5-dimethylaminoindole (Medmain), 1,2-dimethyl-3-ethyl-

Table 1. Antagonistic effect of gramines and aminoindoles on the uterus-stimulant action of 5-HT.

Compound	50% antagonistic dose (μg) to 0.1 μg of 5-HT base
Gramine	3–6
2-Methylgramine	3–6
2-Methyl-5-aminogramine	200
2-Methyl-5-nitrogramine	3–5
2-Methyl-5-chlorogramine	0.3–0.4
2-Methyl-7-chlorogramine	0.5–0.8
2-Methyl-5-bromogramine	0.2–0.4
5,6-Dimethoxygramine	100
3-Diethylaminomethylindole	2–4
2-Methyl-3-pyperidylmethyl-5-chloroindole	4–8
Medmain	6–8
Methylmedmain	3–5
2-Methyl-3-ethyl-5-aminoindole	50–60