physectomy (Table). But the differences in the absolute weights recorded at each dosage level of α-MSH with and without progesterone appear to be a little less marked than in the case of the animals which had undergone castration only; the relative differences, however, i.e. the differences expressed in percentages of the weight of the gland recorded with α-MSH alone, are much the same following castration as following castration and hypophysectomy.

Discussion. The results outlined above deserve comparison with those published by LORINCZ and LANCASTER[6], who demonstrated that a synergistic effect on the preputial glands was exerted by progesterone and a pituitary extract from which the STH, ACTH, and TSH fractions had been eliminated, but whose hormonal composition had not been defined. As regards its influence on the preputial glands, it could seem that STH, while not displaying any synergistic effect with progesterone[6], does exert a synergistic action with testosterone[5]. This type of action, moreover, is not confined to the preputial glands, and a recent study has shown that the ventral prostate can also be stimulated by administering progesterone in combination with LTH[7].

The data obtained in the present series of experiments, coupled with the findings quoted above, serve to highlight the role which peptide hormones may play in modulating the response of certain peripheral receptors to the steroids.

Résumé. L'α-MSH stimule la croissance des glandes préputiales de la rate intacte, cet effet est moins marqué après l'ablation des ovaires et s'atténue encore après castration et surrénalectomie ou castration et hypophysectomie. Chez l'animal castré, en doses liminaires, la progestérone accroît considérablement la stimulation produite par l'α-MSH tandis que la testostérone exerce un effet comparable mais moins accentué. Le synergisme de la progestérone et de l'α-MSH est encore observé, mais légèrement réduit, chez l'animal castré et surrénalectomisé ou castré et hypophysectomisé.

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Administration by Nasal Spray of an 18 Amino Acid Synthetic Polypeptide with Corticotropic Action

The clinical use of ACTH has hitherto been limited by the fact that it could only be given by intramuscular or intravenous injection. Attempts to administer the hormone orally have proved unsuccessful, since, like other proteins, it is denatured by the proteolytic enzymes of the intestinal tract.

For a long number of years, the antidiuretic hormone of the posterior pituitary has been administered by the nasal route. In 1952, SMITH et al.[1] described observations on the effectiveness of nasal insufflation of extractive ACTH. In these investigations, the corticotropic action of ACTH given in powder form was measured indirectly on the basis of the eosinopenic response of the blood.

In the study reported here, a new synthetic polypeptide derived from the ACTH molecule, CIBA 41,795-Ba, was given by nasal spray to normal volunteers, and its corticotropic action was measured directly by reference to the rise in plasma coriticosteroids.

Material and methods. The synthetic polypeptide CIBA 41,795-Ba [D-Ser[1], Lys[17,18]]-β-corticotropin-(1-18)-octadecapeptide amide, was synthesized by RINIKER and RITTEL[2]. It contains the amino acid sequence of the 18 N-terminal amino-acids of ACTH, with the following changes: the first amino acid, serine, is in the D-form instead of the L-form, arginine in positions 17 and 18 is replaced by lysine, and an amide group is present at the carboxyl end of arginine in position 18.

The pharmacology of this polypeptide has been studied by DESAULLES et al.[3,4]. Its action when given by injection to human subjects has been described by WALSER[5,6]; i.m. administration of 1 mg leads to an increase in plasma corticosteroids lasting 24 h.

The subjects taking part in these experiments were normal volunteers, aged between 20–30 years. They had rested for 1 h before the beginning of the tests. In all cases the dose was given at 08.00 h.

The polypeptide administered as a liquid suspension by means of a nebulizing flask which automatically controlled the dose. 6 subjects received a single dose of 0.1 mg. The effect on plasma corticosteroids was followed over a period of 8 h. 5 subjects received 0.3 mg and plasma corticosteroids were subsequently followed over a 6-h period. 12 subjects were treated with a dose of 1 mg. In this group plasma corticosteroids were followed for 4 h in 6 cases and for 12 h in the other 6.

Blood was removed under resting conditions, before and at various intervals after the administration of the product. Plasma corticosteroids were measured according to the method described by PETERSON, KARRER and GUERRA[7].

Results. The means of the plasma corticosteroid levels determined in these subjects after the administration of the various doses are shown in the Table. In the Figure these values are compared with the results obtained in subjects in the same age group receiving no treatment.

As can be seen from these curves, the nasal administration of the 1-18 polypeptide was followed by rise in

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Means of plasma corticosteroid levels after 0.1 mg, 0.3 mg and 1 mg

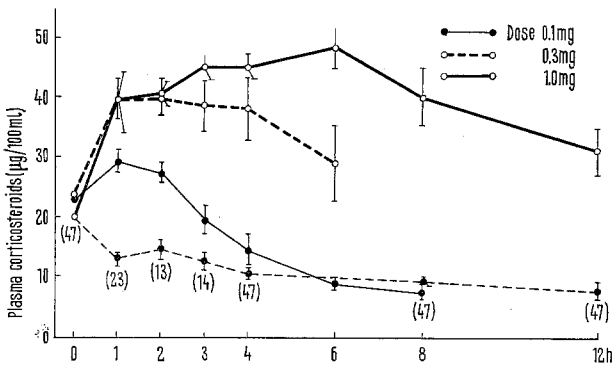
	0	1	2	3	4	6	8	12 h
0.1 mg mean	23.2 (6)[a]	29.6 (6)	27.6 (6)	19.9 (6)	14.7 (6)	9.1 (6)	7.7 (6)	–
S.E.M.	±1.0	±1.7	±1.6	±2.3	±2.5	±1.0	±1.2	–
0.3 mg mean	23.8 (5)	39.7 (5)	40.4 (5)	38.9 (5)	38.2 (5)	29.2 (5)	–	–
S.E.M.	±0.9	±3.4	±3.0	±4.2	±5.2	±6.2	–	–
1 mg mean	20.4 (12)	39.1 (12)	40.7 (12)	45.3 (12)	45.1 (12)	48.8 (6)	40.3 (6)	31.2 (5)
S.E.M.	±2.3	±4.9	±1.8	±2.5	±2.3	±3.7	±4.8	±3.7

[a] (In brackets the number of subjects for each mean value.)

plasma corticosteroids at all the dose levels tested, i.e. 0.1 mg, 0.3 mg and 1.0 mg.

Discussion. In the light of these observations it may be concluded that preparation CIBA 41,795-Ba is fully effective when administered by the nasal route. The dose-response relation is satisfactory.

The duration of action appears to be dose-dependent: the corticotropic effect was still detectable 12 h after the administration of 1 mg of the product, whereas it had already begun to diminish after 4 h following a dose of 0.1 mg.



Curves of plasma corticosteroid levels after the various doses tested. The dotted line represents the diurnal rhythm of normal non-treated subjects (in brackets the number of subjects for each mean value).

This study shows that, despite the individual differences in response normally attendant upon the use of nasal sprays, the corticotropic action of the peptide administered in this way is remarkably consistent. At any given dose the statistical scatter is small.

The administration of a polypeptide with corticotropic activity by the nasal route would thus appear to offer a means of circumventing the difficulties associated with repeated administration by injection[8].

Résumé. L'administration en nébulisation nasale d'un peptide synthétique corticotrope: [D-Sér[1], Lys[17,18]]-β-corticotrophine-(1-18)-octadécapeptide$_o$amide (CIBA 41,795-Ba), s'est montrée parfaitement efficace et a élevé le taux des corticoïdes plasmatiques chez des volontaires normaux. La relation dose-réponse s'est montrée très satisfaisante.

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Cytochemical Studies on Histone Moiety of an Asynaptic Mutant of *Phaseolus mungo*

On the basis of cytophotometric studies, ANSLEY[1,2] reported that, compared with the normal meiotic cells, the asynaptic cells in *Loxa* and *Scutigera* produce an increased amount of histone. The availability of an asynaptic mutant of *Phaseolus mungo* prompted the present investigation on the histones of normal and asynaptic plants.

Materials and methods. The root tips and the microsporocytes of the normal and the mutant plants were stained with alkaline fast green after TCA hydrolysis[3] and bromphenol blue and eosin Y after picric acid hydrolysis[4]. Acetylation and deamination of histones were also carried out prior to staining to determine whether the histones are rich in arginine or lysine[4]. The degree of stainability was assessed by visual rating of coded slides by 2 different individuals.

Results and discussion. When the root tip cells of the normal and asynaptic plants are stained with alkaline fast green, nucleoli and chromatin matter of both the plants stain uniformly. Acetylation and deamination of

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