	No. Dogs	Hydrocortisone Equivalents	
		μg/ml	μg/2 min
Normal $\pm$ S. D. with Conf. limits, P = 0·01 . .	86	3·6 $\pm$ 1·8 (4·12 — 3·12)	14·0 $\pm$ 6·5 (15·81 — 12·15)
Su 4885 $\pm$ S. D. with Conf. limits, P = 0,01 . .	6	1·1 $\pm$ 0·8 (2·37 — 0)	4·6 $\pm$ 2·9 (9·44 — 0)

(*D*) *Other Endocrine Actions.*—Su 4885 (free base-subcutaneous) was not progestational at 50 mg/kg/day when tested according to the Clauberg technique in rabbits. Neither did it affect the weights of seminal vesicles, testes or uteri in rats in doses of 30–130 mg/kg when given orally or subcutaneously for 3–5 days.

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Research Department, CIBA Pharmaceutical Products Inc., Summit (N. J.), December 24, 1957.

Zusammenfassung

2-Methyl-1,2-bis-(3-pyridyl)-1-propanon (Su 4885) hemmt beim Hund die Ausscheidung von 17-OH-Steroiden aus den Nebennieren und hemmt *in vitro* ähnlich wie Amphenon den ACTH-Effekt auf Ratten-, Meerschweinchen- und Hunde-Nebennieren. *In situ* bei der Ratte hat es jedoch keine Amphenon-Wirkung, von dem es sich auch sonst unterscheidet.

Stress Response of Leucocytes in Hypothyroid Rats

The relations between adrenal and thyroid glands occupy an important place in the hormonal regulations of the organism. The great part of them has the character of antagonistic influence on various functions[1]. However, the intimate relationship between these two glands remains on the whole unresolved.

We examined the influence of thyroid on the regulation of nonspecific stress response of leucocytes in rats by means of competitive inhibition of thyroid function. In distinction from the majority of experiments using thyroidectomy or strumigen feeding, we applied low doses of dried thyroid gland in order to cause hypofunction of the thyroid gland. Each of a group of white rats, males (n = 30), was given a daily dose of 20 mg dried thyroid gland (Thyreoidin SPOFA). The mean weight of this group (210 g) fell to 180 g after 36 days feeding. The mortality was 10%. The feeding by thyroid gland was stopped on the 37th day and the rats were kept for the next 7 days on normal food. During this period, the weight reached the level of the control non-treated group (n = 30) kept on normal diet. On the 8th day after the stopping of thyroid feeding, 6 of treated animals and 8 of the control group were killed and the thyroid, thymus and spleen were examined histologically. At the same time the leucocytes number and differential count were determined. The histological examination of thyroid in the treated group revealed the lowering and occasionnally the degeneration of follicular epithelium (Fig. 1 and 2). The histological picture of the thymus and the spleen were essentially the same as in the control group. In the peripheral blood, no important differences were found in the total number of leucocytes (M = 8500), neutrophils (M = 3000), lymphocytes (M = 5500) and eosinophils (M = 370).

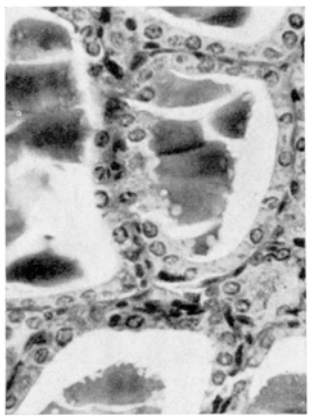

Fig. 1.—Thyroid of the control non-stressed rat. × 340.

The rest of the treated and control animals was given the intramuscular formaldehyde injection (0·5 ml 4%) and the animals were killed after 3 h (2 + 2), 6 h (2 + 2), 12 h (2 + 2), 24 h, (8 + 8) and 48 h (8 + 8). The blood leucocytes, thymus, and spleen were examined. The graphs illustrate the changes of neutrophils, lymphocytes and eosinophils. The stress deviations of the mean values are expressed in % of the mean initial value (= 100%) of the non-stressed animals. The statistical significance of the differences in the course of the stress response was determined by T test from the differences of the absolute values.

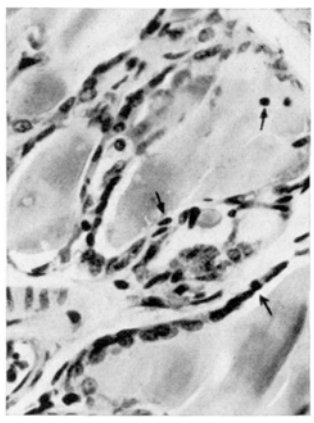

Fig. 2.—Thyroid of the non-stressed rat from the group feeded on thyroid gland before the beginning of the experiment. Follicular epithelium is lowered and occasionally degenerated (→). × 340.

Figure 3 shows the changes of neutrophils, and Figure 4 the changes of lymphocytes and eosinophils during the stress. The stressed control animals exhibit the changes typical for Selye's alarm reaction. The group with thyroid

[1] A. ALBERT, Ann. Rev. Physiol. *14*, 481 (1952).

hypofunction is distinguished by the following characteristic differences. The initial neutrophils peak was supressed without any influence on lymphopenia and eosinopenia, and in the same way the lymphocytes and eosinophils increase was inhibited in the subsequent intervals. Therefore the hypofunction of the thyroid seems not to influence the lymphopenic and the eosinopenic phase of the stress. However, it is not possible to draw any definitive conclusion from a small number of animals killed at intervals. But the inhibition of the increase of neutrophils, lymphocytes and eosinophils was proved very definitely.

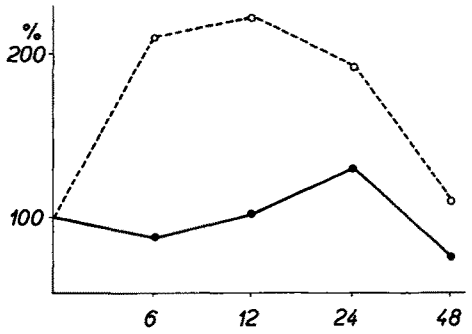

Fig. 3.—The stress changes of neutrophils in the control group (interrupted line) and in the hypothyroid group (full line). The ordinate shows the leucocytes deviation in %, the abscissa indicates the time of examination in hours after the evocation of stress.

The differences were statistically significant. $P < 0{\cdot}02$ expresses the significance of differences in neutrophils comprising the values of 6th and 12th h; $P < 0{\cdot}02$ denotes the significant difference of lymphocytes of both group comprising the values of the 12th and 24th h; $P < 0{\cdot}01$ denotes the significance of differences of eosinophils at 24th h.

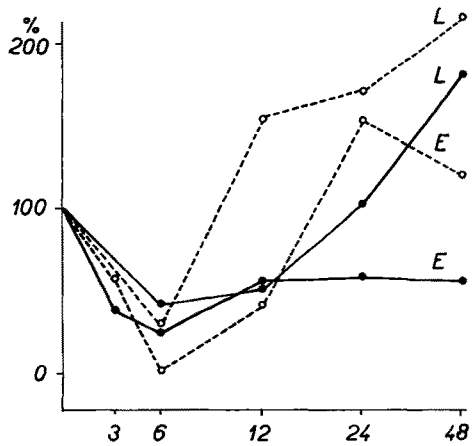

Fig. 4.—The stress changes of lymphocytes (L) and eosinophils (E) in the control group (interrupted line) and in the hypothyroid group (full line), expressed in % of the mean initial value.

There were no differences in the degree of lymphocytes fragmentation between the control and hypothyroid group in the thymus. In the spleen of the control rats, the fragmentation of lymphocytes was followed by the rise of activity in secondary lymph nodules as judged by the characteristics of their light centres[2]. In contract to this the spleen of hypothyroid rats showed much less intensity of lymphocytes fragmentation, and the successive rise in the activity of centres was absent. In this connection it is necessary to mention the studies by GYLLENSTEN in which the lymphatic hyperplasia in the guinea pigs was evoced by thyroxine[3].

We may conclude that the rats with lowered function of thyroid gland after chronic thyroid feeding show deviation in the stress response of leucocytes. This deviation manifested itself in the prevention of increase of neutrophils, lymphocytes and eosinophils. The rise of activity in secondary nodules of the spleen was also inhibited.

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Zusammenfassung

Nach Formalininjektion zeigen mit getrockneter Schilddrüse gefütterte Ratten eine Abweichung der peripheren Leukocytenreaktion. Bei so behandelten Ratten mit Schilddrüsenhypofunktion ist die Vermehrung der Neutrophilen, die Lymphocytose und die Eosinophilie gehemmt. Auch die histologische Kontrolle ergab eine Hemmung der transitorischen Aktivitätssteigerung des lymphoretikulären Milzgewebes.

[2] M. HILL and M. POSPÍŠIL, to be published, 1958.

[3] L. GYLLENSTEN, Acta Anatomica 17, Suppl. 18, 1 (1953).

Zur Biogenese pentazyklischer Triterpene in einer höheren Pflanze

Die Gültigkeit der Squalenhypothese bei der Biogenese von Cholesterin und anderen Steroiden (Zymosterin, Ergosterin u.a.), sowie von tetrazyklischen Triterpenen der Lanosteringruppe (Lanosterin und Eburicolsäure) bei Mikroorganismen, Pilzen und höheren Tieren ist durch zahlreiche Arbeiten von BLOCH und anderen Autoren wiederholt bestätigt worden.

Alle diese tetrazyklischen Verbindungen sind durch einen weitgehend übereinstimmenden räumlichen Bau charakterisiert. Die Squalenhypothese wurde auch herangezogen zur Deutung der Biogenese der anderen, mit Lanosterin stereoisomeren tetrazyklischen Triterpengruppe (Tirucallol, Euphol u.a.), sowie der zahlreichen pentazyklischen Triterpenverbindungen, für die das Vorkommen im Pflanzenreich besonders charakteristisch ist[1].

Die Übertragung der Squalenhypothese auf diese Verbindungen, die zuerst auf einem Vergleich der verschiedenen Kohlenstoffgerüste beruhte[1] und die man später durch stereoelektronische Betrachtungen stützen konnte[2], wurde bisher noch nicht einer experimentellen Prüfung unterzogen. In der vorliegenden Mitteilung werden die ersten Ergebnisse einer in dieser Richtung unternommenen Arbeit beschrieben.

[1] L. RUZICKA, A. ESCHENMOSER und H. HEUSSER, Exper. *9*, 357 (1953).

[2] A. ESCHENMOSER, L. RUZICKA, O. JEGER und D. ARIGONI, Helv. chim. Acta *38*, 1890 (1955). – L. RUZICKA in A. TODD: *Perspectives in organic chemistry* (Interscience Publishers Inc., New York und London 1956), S. 265.