The increase in uterine water content following oestradiol administration[1,2,4] and the concomitant rise in Na^+ and fall in K^+ concentrations between 6 and 8 h after the administration of oestradiol[1,2] could be a consequence of the fall in ATPase activity observed in these experiments. There is some evidence that the Mg^{++} activated ATPase is a component of the Na^+ pump mechanism[5].

MEANS and HAMILTON have reported an increase in protein synthesis which is preceded by stimulation of both the synthesis of nuclear RNA and uptake of RNA precursors in the uterus within 2 min following administration of oestradiol-17β to ovariectomized rats[6]. Thus although oestrogens are capable of stimulating net protein synthesis in the uterus by increasing the rate of formation of template RNA, the present work suggests this is not a universal effect in uterine proteins and that a loss of ATPase accompanies these changes. Although this could represent a direct interaction of oestrogen and enzyme, the delay in onset of the effect suggests a selective inhibition of synthesis of enzyme protein[7].

Zusammenfassung. 17-β-Östradiol wirkt am Rattenuterus hemmend auf die ATPase, von der bekannt ist, dass sie auf die sogenannte Natriumpumpe in der Zelle wirkt.

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Persistence of a Physiological Circadian Rhythm of Plasma-Free 11-Hydroxycorticosteroid Levels in Totally Fasting Obese Subjects

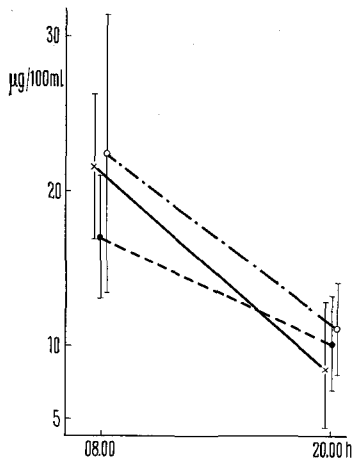
Rhythmic variations of pituitary ACTH output are the likely explanation for the high early morning and the low late evening levels of blood cortisol concentrations[1]. The physiologic pattern of circadian variations of plasma cortisol levels may be disturbed by numerous conditions such as psychic stress, central nervous disease and a wide variety of acute and chronic illnesses (for a review see SAWIN[2]).

Thus, it was tempting to speculate that long-lasting severe fast in obese subjects, a rather well-defined procedure associating considerable psychological stress with tremendous metabolic upset, would also interfere with normal pituitary-adrenal function.

In order to put this hypothesis to the test the normal circadian rhythm of free plasma 11-hydroxycorticosteroid levels (further referred to as 'cortisol') was first determined by fluorimetrically[3] measuring blood steroids at 08.00 and 20.00 in a group of 21 healthy young volunteers instructed to adhere to their normal activity schedule. The mean cortisol levels were: 21.8 ± 4.8 µg/100 ml at 08.00 and 8.7 ± 4.2 µg/100 ml at 20.00 (mean decline $60.6 \pm 15.9\%$). All individuals had definitely lower values in the evening than in the morning.

The same procedure was then applied in 8 hospitalized obese patients whose characteristics are given in the Table. The patients were subjected to a program of physiotherapy and active physical training. Again a rather uniform pattern of steroid rhythm was found. After total starvation (6 subjects) or 600 Cal. intake (2 subjects) for 16–33 days with a mean weight loss of 8.8 kg the patients again had their morning and evening blood steroid levels measured. In the Figure the mean decline of the evening values before and after starvation is indicated: The pattern remains rather identical, except for patient B.T. (not included in the Figure). In this case the diurnal rhythm became reversed. However, this patient's fast led to complications such as severe E.C. volume depletion, hypotonia and hypokaliemia which prompted precocious termination of total starvation.

Furthermore, it can be seen in the Table that the mean values for absolute 'cortisol' concentrations in



Circadian rhythm of free 11-hydroxycorticosteroid concentration (mean values ± 1 S.D.) in the blood of normal non-obese controls (×), obese patients before fasting (●) and at the end of a therapeutic fast (○). The evening cortisol levels are significantly lower than the morning levels in all 3 groups of subjects ($p < 0.005$). There is no significant difference between the 3 groups.

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Summary of relevant data collected from obese patients treated with total or partial (600 Cal.[a]) fast

Name	Sex	Age	Height cm	Weight kg	Days of fast	Total wt. loss	Mean daily wt. loss	Plasma cortisol μg/100 ml before fast 08.00	before fast 20.00	before fast %	after fast 08.00	after fast 20.00	after fast %
B. T.	f	37	166	102.8	33	13.8	0.42	21.3	8.1	38.1	24.4	28.5	116.8
C. M.	f	63	161	87.2	22	9.3	0.42	11.6	7.0	60.3	41.6	15.4	37.0
K. R.	f	16	167	107.6	29	12.0	0.41	15.1	9.8	64.9	18.5	6.9	37.3
M. E.	f	23	163	105.4	16	6.7	0.42	16.1	14.8	91.9	16.3	8.8	54.0
E. W.	m	21	176	105.5	17	10.7	0.63	19.9	8.4	42.4	22.6	11.1	49.1
F. W.	m	33	181	95.0	19	9.2	0.48	24.3	10.8	44.4	23.2	11.0	47.8
S. E.[a]	f	59	166	141.1	22	4.8	0.22	15.3	6.5	42.5	13.3	9.4	70.7
M. A.[a]	m	59	168	83.0	23	8.7	0.38	17.2	13.7	79.7	23.4	14.9	63.7
mean values (patient B. T. not included)				103.5	21	8.8	0.42	17.1	10.1	60.8	22.7	11.1	51.4
							± S.D.:	4.1	3.2	19.6	9.2	3.1	12.6

morning and evening blood samples were the same before and after fasting. The values did not differ from steroid levels found in normal subjects.

The data show that methods currently used for assessing pituitary-adrenal function fail to show any consistent change in obese patients starved for prolonged periods of time. The finding is somewhat unexpected since obesity by itself has been claimed to be associated with abnormal adrenal function[4–10]. Moreover, adrenal hyperfunction as well as hypofunction have been repeatedly described as being a consequence of starvation and undernutrition. For instance, TALBOT et al.[11] found decreased pituitary activity in malnourished children. Similar findings were reported by COOKE et al.[12], PERLOFF et al.[13], HUSEBY et al.[14], NEUWIRTH et al.[15] and many others. These reports are in keeping with the findings of a picture indistinguishable from pituitary insufficiency in anorexia nervosa[16,17].

On the other hand, recent investigations on blood and urinary steroid levels in children with severe malnutrition[18] confirmed earlier findings of GILLMAN et al.[19] who found adrenal hyperfunction at least in the initial phase of starvation.

It is somewhat puzzling to realize that a great many non-endocrine diseases do disturb pituitary-adrenal function, whereas the heavy metabolic upset forced upon a starving obese patient[20–22] does not. From a survey of the literature and from analysis of the present data, as well as from one other somewhat similar study reporting on shorter periods of fast (SCHACHNER et al.[23]), one must conclude firstly that no consistent abnormality of adrenal function occurs in obese patients, and secondly that this gland continues to function normally even after long-lasting severe fast. Therefore, if steroid rhythms do show abnormal patterns, one must look for one of the many complications not infrequently occurring in prolonged fasting (see subject B.T.). This could well account for the inconsistent findings on cortisol blood levels reported by LINQUETTE et al.[24].

Zusammenfassung. Die physiologische rhythmische Aktivität der Nebennierenrinde ist auch bei adipösen Patienten nachzuweisen. Selbst 16–33tägiges totales (6 Patienten) oder partielles (2 Patienten) Fasten vermag den Tagesrhythmus der Kortisolsekretion nicht zu verändern. Jede Abweichung von der Norm weist daher auf eine Komplikation der Fastenkur hin.

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