THE URINARY EXCRETION OF 17-KETOSTEROIDS IN PEMPHIGUS FOLIACEUS*

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The work of a few investigators over a decade ago described a disturbance in water and salt metabolism in pemphigus and suggested an adrenal dysfunction as the basic physiopathologic change in this disease (1–4). Pathologic findings in the adrenal glands at necropsy, although rare, were also quoted in suport of this view (5, 6). Most papers referred to pemphigus vulgaris, in the acute or chronic forms. In regard to pemphigus foliaceus there was only a reference to 4 patients studied by Lever and Talbott (4) besides the paper of one of us (T.A.F.) and Brandão (7), reporting that biochemical studies and post-mortem observations were not conclusive as to an etiologic role of the adrenals in this disease.

Interest in the subject was recently stimulated since the observation of the favorable response of pemphigus to adrenocorticotropic and corticoid hormones. Progress in methods of study of adrenal function made possible new lines of research. Almeida (8) perfomed the 4-hour ACTH test of Thorn *et al.* (9) in 18 male and in 7 female patients with pemphigus foliaceus and found an absence of eosinopenic response in 64% of the cases, which he consider a sign of adrenocortical hypofunction. Caccialanza *et al.* (10) made the dosage of urinary excretion of reducing corticoids and 17-ketosteroids in 15 patients (8 with pemphigus vulgaris, 1 with pemphigus erythematosus, 1 with pemphigus vegetans and 5 with dermatitis herpetiformis) finding subnormal figures in some of the patients, with values lowest in long-standing cases. There was no apparent difference between pemphigus and Duhring's disease. However, a difference in response was noted after stimulation with ACTH: in pemphigus values were low and even lower than those found in basal conditions, where as in dermatitis herpetiformis the excretion of the reducing corticoids was greatly increased. Quiroga and Corti (11) found 17-ketosteroid levels consistently decreased in 8 cases of pemphigus vulgaris and in 4 out of 5 cases of pemphigus foliaceus, and ascribed importance to this dosage in the differential diagnosis of pemphigus with other bullous disease. Cohen *et al.* (12) examined the 24-hour urinary excretion of 17-ketosteroids in 8 patients suffering from pemphigus vulgaris obtaining values between 4.7 and 12 mg, somewhat below the normal average found in the laboratory in which the tests were perfomed. Xavier *et al.* (13) found in 9 patients with Brazilian pemphigus foliaceus (Fogo selvagem) 0.1 to 1.7 mg per day and in 1 patient with pemphigus vulgaris acutus 2.1. However, these authors did not find any correlation between the very low figures of 17-ketosteroids and the clinical course of the disease.

This is part of a paper read before the XV Annual Meeting of the Brazilian Dermatological Society, Belo Horizonte, Brazil, July 7–11, 1958.

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Received for publication October 13, 1958.

MATERIAL AND METHODS

The investigation was carried out in 21 patients with pemphigus foliaceus hospitalized in the Dermatologic Clinic of the Faculty of Medicine of the University of Minas Gerais. In all cases the clinical diagnosis was confirmed by histopathological examinations.

The dosages of the 24-hour urinary excretion of 17-ketosteroids were performed according to the method of Drekter *et al.* (14) with slight modifications suggested by Antunes (15). Normal values by this method are 10 to 20 mg for male, 5 to 15 mg for female and an average of 4 mg for children from 7 to 12 years of age. For each patient two dosages were used, the results showing an average difference of 0.3 per 24 hours.

RESULTS

The results of the urinary excretion of 17-ketosteroids are represented in Table I. The dosages gave figures below the normal in 61.8 per cent of the cases. However in most cases there were only slight deviations from the normal. Four out of

TABLE I

Number and Name	Age—Years	Sex	Duration of Disease	Last Shower of Bullae (months)	Sedimentation Rate (Westergren-mm/hour)	General Condition	Present Treatment	Urinary Volume in 24 Hours (ml)	17-Ketosteroids (mg)
1. MAC	16	F	9 ms	9	10	Excellent	Sulfamides	1,240	8.2
2. MNS	25	F	8 ys	Present	6	Good	Local	1,600	7.4
3. ZMJ	19	F	11 ys	1		Good	Antimalarial drug	1,300	3.6
4. AAR	36	F	6 ms	1	56	Poor	Triamcinolone	2,330	5.4
5. MLS	14	F	3 ys	10		Poor	Local	1,200	3.6
6. ECE	46	F	4 ys	3	55	Good	Local	2,180	7.8
7. NMG	55	F	7 ys	3	60	Fair	Antimalarial drug	2,230	4.0
8. GBJ	40	F	33 ms	29	50	Good	Local	1,980	5.9
9. NGL	37	F	20 ms	Present	88	Fair	Cortisone	1,480	1.9
10. MAJ	17	F	2 ys	Present	48	Good	Sulfamides	2,000	3.7
11. MEDS	16	F	4 ms	Present	80	Fair	Triamcinolone	1,000	3.0
12. MGT	9	F	6 ys	Present	7	Fair	Sulfamides	570	1.6
13. IBS	21	F	43 ms	Present	5	Good	Local	1,540	3.5
14. MLL	26	F	30 ms	4	28	Good	Sulfamides	1,270	4.5
15. JBP	23	M	4 ys	Present	20	Fair	Triamcinolone	3,930	3.2
16. AMA	22	M	9 ms	Present	15	Poor	Local	370	4.0
17. JPR	17	M	8 ms	Present	3	Poor	Cortisone	1,400	8.3
18. AMR	28	M	6 ys	3		Good	Local	2,700	12.6
19. VPM	25	M	10 ys	1		Good	Local	1,760	13.0
20. GACV	21	M	4 ys	8		Excellent	Local	1,580	11.3
21. MSM	24	F	11 ys	4		Excellent	Antimalarial drug	820	3.8

five patients under steroid therapy also exhibited subnormal values, which were not lower than those from patients under other types of treatment.

COMMENTS

All patients had the generalized form of the disease, according to the classification of Vieira (16), Rabello (17) and Orsini (18). In this study there are no cases of pemphigus erythematosus, which we consider a *forme fruste* of pemphigus foliaceus.

These results did not show any correlation between the figures obtained and the cutaneous and general conditions of the patients studied. Only 1 patient whose condition was poor had normal excretion of 17-ketosteroids, but the status from 13 with subnormal values was fair in 5, good in 4 and excellent in 1.

It should be pointed out that, with one exception, all patients who had bullae, indicating activity of the disease process, gave low values.

It is a known fact that there is adrenal depression during cortisone therapy, which is explained by Ingle and Baker (19) as a consequence of the involution of the *zona fasciculata* of the adrenal cortex by supressing the endogenous secretion of ACTH. However the figures obtained in 4 patients under cortisone therapy were not lower than those from patients with other type of treatment and in one patient was even normal.

The results of the present investigation are in agreement with our previous work (7), according to blood values of sodium and potassium.

From our present knowledge of the subject we are not allowed to talk of an adrenal disfunction having an etiologic role in pemphigus foliaceus. What seems to occur in this disease as well as in others of infectious or toxic nature, is an increase in the requirements of adrenocortical hormones by the organism, far in excess of the physiological amounts, due to the continuous stress represented by a chronic and serious disease like pemphigus. The patients whose glands are unable to meet this daily increased demand as well as the emergencies of the frequent recurrences, would exhaust their reserve and show a relative insufficiency. These patients have a functional adrenal hypofunction.

SUMMARY

The 24-hour urinary excretion of 17-ketosteroids was determined in 21 patients with clinical

and histological diagnosis of pemphigus foliaceus. The values were subnormal in 13 patients (61.8%) and normal in 8 patients. There was no correlation between the figures obtained and the clinical and cutaneous course of the disease. The low values may be explained by an inability of the adrenal glands to meet the increased daily requirements of hormones by the organism submitted to a continuous stress represented by a chronic and serious disease like pemphigus foliaceus.

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