Adrenal Cortex in Marasmic Children*

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The effect of malnutrition on the adrenal cortex has not been well studied. Earlier reports suggested that malnutrition in man produced adrenocortical hypofunction (Zubirán and Gómez-Mont, 1953), and more recent reports suggest normal function (Lurie and Jackson, 1962) and possibly hyperfunction of the adrenal cortex in malnourished infants (Alleyne and Young, 1966). The purpose of this study was to assess the effect of the marasmic type of malnutrition on the integrity and functional reserve of the adrenal cortex using the ACTH stimulation test (Liddle, Estep, Kendall, Williams, and Townes, 1959).

Subject and Methods

Sixteen marasmic infants 4 to 18 months old were studied. The cause of malnutrition in all 16 was primarily undernutrition, aggravated in most by gastro-intestinal disturbances. None had the changes found in kwashiorkor. 12 weighed less than 60% of their ideal weight, the other four weighed between 60 and 75% of their ideal weight and were classified as suffering from third and second degree malnutrition, respectively (Gómez, Galván, Cravioto, and Frenk, 1955). That these children suffered primarily from undernutrition is evidenced by the wide discrepancy between their respective heights and weights.

The studies were performed soon after admission of these infants to either the Sidon Government Hospital or the Solarium Hospital, and before adequate dietary replenishment was started. In the main, boys were used in this study because of the relative ease of collecting complete 24-hour urine samples. No infant suffering primarily from a disease besides malnutrition was included.

ACTH test. A 24-hour urine sample was collected to serve as baseline control, then each infant received ACTH-zinc intramuscularly, 20 units every 12 hours, for 3 days. Urine was collected during the last day of ACTH administration. 17-hydroxycorticosteroids (17-OHCS) levels were determined in each 24-hour urine specimen by the method of Reddy (1954).

Results

The results of the ACTH stimulation are shown in the Table. All but one of the 16 infants (Case 14) responded very well to ACTH administration. They increased several fold their basal urinary 17-OHCS excretion. It is worth noting that Case 14 was one of the two least malnourished children.

Discussion

The effect of malnutrition on adrenal function cannot be evaluated properly unless production rates of the hormones secreted are determined. In malnourished subjects, however, a significant increase in the urinary or plasma metabolites of cortisol in response to adequate exogenous ACTH stimulation indicates that malnutrition has no direct adverse effect on the adrenal cortex; any adrenal hypofunction that may be present under such circumstances must then be secondary to the effect of malnutrition on the anterior pituitary rather than a primary effect on the adrenal cortex.

Our study demonstrates that the adrenal cortex of marasmic infants, when provided with an adequate stimulus, shows no evidence of insufficiency or decreased functional reserve in so far as cortisol production is concerned. This is in contrast to the finding of Monckeberg, Beas, and Perretta (1956) and Castellanos and Arroyave (1961). The former observed only a slight increase in the urinary 11-oxysteroid excretion in 10 malnourished infants following 5 days of ACTH stimulation. The degree of malnutrition of these infants was similar to that of our group. The difference, however, can be attributed to the non-specific method used by these investigators to measure the urinary metabolites of cortisol by measuring the 11-oxysteroid. This is evidenced in the failure of their 6 normal controls to triple their urinary excretion of 11-oxysteroids after ACTH stimulation, while in our study the increase in urinary 17-OHCS averaged more than tenfold. Castellanos and Arroyave (1961) reported that ACTH stimulation failed to increase the already

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TABLE
Increase in Urinary 17-Hydroxycorticosteroids After ACTH in Marasmic Infants

Case No., Sex, and Age (mth.)	Weight		Height		Urine 17-OHCS (mg./day)	
	Grams	% Normal	Cm.	% Normal	Control Day	3rd Day of ACTH
<i>Third Degree Malnutrition Group</i>						
1 M 16	5200	48	70	89	2.27	19.0
2 M 18	6300	56	66	80	1.33	9.0
3 M 7	4600	56	47	70	0.53	10.8
4 M 10	5400	55	66	91	0.35	10.5
5 M 7	4400	56	61	92	3.5	12.0
6 M 9	4800	54	63	90	0.26	17.0
7 M 5	2800	41	58	92	0.40	16.2
8 M 6	3640	45	53	80	1.0	20.0
9 F 6	2600	25	55	85	0.45	8.0
10 F 10	3700	40	62	87	0.0	6.5
11 M 5	3300	47	—	—	0.44	5.2
12 M 4	3000	48	—	—	0.51	9.9
Mean 8.5	4145				0.92 ($\pm 0.088^*$)	12.0 ($\pm 0.83^*$)
<i>Second Degree Malnutrition Group</i>						
13 M 6	5400	74	66	100	1.15	14.64
14 M 5	4800	70	58	92	1.19	3.6
15 M 5	4300	64	55	87	0.44	5.22
16 M 5	4750	70	—	—	1.60	13.0
Mean 5.25	4800				1.08 ($\pm 0.24^*$)	9.1 ($\pm 2.75^*$)

* Standard error of the mean.

high levels of 17-OHCS excretion in the urine of 5 infants with marasmus. They postulated that the adrenal cortex was under maximal stimulation in these infants. These authors, however, collected urine for only 12 hours 'in most of the cases' and calculated the 24-hour excretion of 17-OHCS on this basis. The known diurnal variation in the urinary excretion of cortisol metabolites, with maximal excretion in the early hours of the day, may have spuriously raised their baseline values. Moreover, they only administered 10 units of ACTH gel once, which might not have been a sufficient stimulus for the adrenals, particularly if these have not been under adequate endogenous ACTH stimulation. On the other hand, 3 of the 4 marasmic infants reported by Lurie and Jackson (1962) had an adequate response to ACTH, and more recently Alleyne and Young (1966) showed that children with 'protein-calorie' malnutrition had higher plasma levels of 11-hydroxycorticosteroids and a greater response to 'synacthen' (B^{1-24} corticotrophin) than those who had already recovered from malnutrition. Similarly, adequate response to ACTH stimulation was found in children with the kwashiorkor type of infantile malnutrition (Castellanos and Arroyave, 1961; Lurie and Jackson, 1962), as well as in women suffering from anorexia nervosa (Bliss and Migeon, 1957; Fletcher and Brown, 1959; Marks and Bannister, 1963). From these observations it can be concluded that the capacity of the adrenal cortex to secrete cortisol, when provided with an adequate stimulus, is not affected adversely by the various

types of malnutrition. Actual production rate of cortisol in malnutrition, however, awaits further investigations.

Summary

Sixteen marasmic infants were tested for adrenocortical function using the ACTH stimulation test. The results indicate that malnutrition does not lead to adrenal insufficiency or decreased functional reserve.

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