Integrity of the Hypothalamo-Pituitary-Adrenal Axis in Kwashiorkor as Tested with Piromen

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SUMMARY

Plasma cortisol levels were determined in 30 kwashiorkor children with and without Piromen stimulation on admission to hospital, after 1 week and after 5 weeks. A positive response after Piromen injection was considered to be present if there was an increase in cortisol level of 50% or more above the basal value. The incidence of responders was similar on admission and after 5 weeks. There were, however, fewer responders one week after admission than either at the beginning or at the end, the reaction appearing somewhat blunted at this stage.

Plasma cortisol levels could not be related to the degree of body weight deficit, haemoglobin concentration, serum albumin reduction or total number of white blood cells. It is concluded that the hypothalamo-pituitary-adrenal interrelationship does not appear to be particularly disturbed in uncomplicated kwashiorkor.

S. Afr. Med. J., **48**, 2303 (1974).

In developing countries loss of life due to severe protein energy malnutrition continues to be formidable. Factors pertaining to the short-term prognosis of kwashiorkor include severe dermatosis, gross hepatomegaly, increased serum bilirubin levels, hypothermia, hypoglycaemia and septicaemia.[1-4] In view of the vital role of the endocrine glands, especially that of an intact hypothalamo-pituitary-adrenal axis in stress situations, it was deemed appropriate to evaluate further the integrity of the axis in kwashiorkor patients.

PATIENTS AND METHODS

Thirty children suffering from classical kwashiorkor were studied. Only patients uncomplicated by clinically apparent infections were selected. The hypothalamo-pituitary-adrenal axis was assessed by means of intravenous Piromen (Travenol Laboratories, Morton Grove, Ill., USA), which has a specific activating effect on ACTH release.[5] Plasma cortisol levels were determined (Cea-Cen-Sorin kit—competitive protein binding method) on blood samples taken at the following three times:

On admission (within 1 - 3 days) a basal specimen at 0800, followed immediately by the intravenous injection of Piromen in a dose of 0,5 μg/kg. Blood samples were again collected 2 hours later and in many patients also 4 hours later to determine the cortisol response.

On the next day, a basal specimen at 0800, a specimen at 1600 and in a number of patients also at 2200, were taken to determine the circadian rhythm.

One week (7 - 10 days) after admission to hospital the above procedure was repeated.

After clinical recovery (35 - 42 days after admission) the procedure was again repeated.

The serum albumin, haemoglobin, total white blood cell values and the percentage expected body weight were also determined on admission and after recovery. (The Boston 50th percentile value was taken as expected weight.)

RESULTS AND DISCUSSION

One patient with a very high basal plasma cortisol concentration of 144 μg/100 ml had superimposed acute pyelonephritis and was excluded from the study. The data pertaining to the remaining 29 patients are represented in Table I and in Fig. 1.

In order to find out whether significant differences existed between values on admission, after 1 week and after 5 weeks, the data were compared separately for each of the times 0800, 1000 and 1200. The statistical test utilised was a two-way analysis of variance (mixed model).[6] Computations indicated a significant F-value ($P<0,01$) only in the case of the 1000 values. By means of Scheffe's multiple comparisons method[6] it was then found that after 1 week the 1000 values differed significantly from the comparable levels on admission and after 5 weeks. The fact that the 1200 values after 1 week did not differ from comparable values on admission and after 5 weeks could have been due to the smaller number of observations at this interval.

The patients were divided into cortisol responders or non-responders, considering an increase of 50% or more at 1000 above the basal level at 0800 as a responder to Piromen stress. Sixty-seven per cent of them responded on admission, 41% after 1 week and 71% after clinical recovery (Table II). Considering the incidence of non-responders after 1 week as well as the significantly lower cortisol levels at 1000, the reaction appeared somewhat

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Date received: 1 August 1974.

TABLE I. CORTISOL LEVELS (μg/100 ml) OF KWASHIORKOR PATIENTS BEFORE AND AFTER PIROMEN STIMULATION ON ADMISSION, AFTER 1 WEEK AND AFTER 5 WEEKS

Time		Period		
		On admission	After 1 week	After 5 weeks
0800 (immediately before Piromen)	Mean	19,3	15,5	14,3
	Standard deviation	8,96	5,44	7,31
	No. of patients	29,0	28,0	27,0
1000 (2 h after Piromen)	Mean	35,4	23,9	29,6
	Standard deviation	17,76	12,97	13,78
	No. of patients	29,0	28,0	27,0
1200 (4 h after Piromen)	Mean	35,1	26,6	23,8
	Standard deviation	24,91	13,80	9,50
	No. of patients	17,0	16,0	15,0

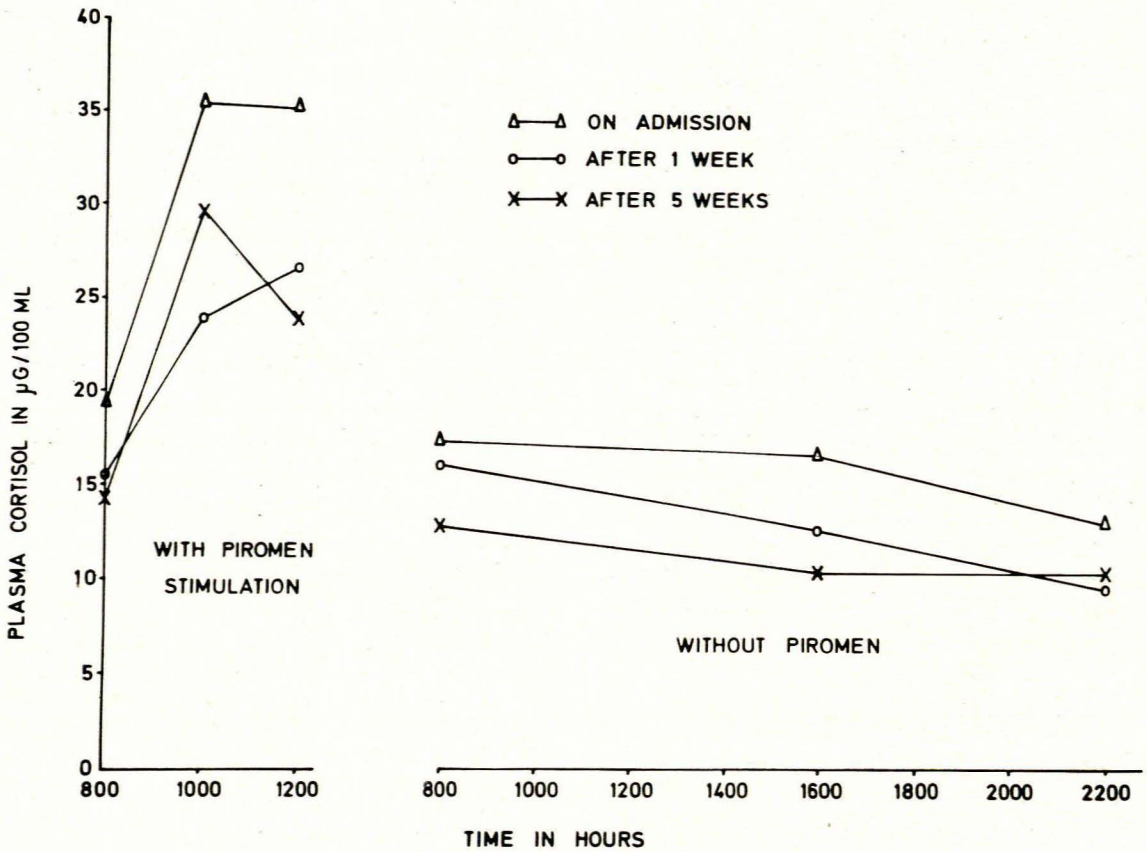

Fig. 1. Plasma cortisol levels in kwashiorkor patients with and without Piromen stimulation on admission, after 1 week and after 5 weeks.

TABLE II. INCIDENCE OF RESPONDERS AND NON-RESPONDERS

	On admission	After 7 days	After 5 weeks
Responders	20 (67%)	12 (41%)	20 (71%)
Non-responders	10 (33%)	17 (59%)	8 (29%)

blunted at this stage. No suitable explanation can, however, be offered for this phenomenon. No significant differences could be found between responders or non-responders considering the degree of underweight, serum albumin or haemoglobin values, or their total number of white blood cells (Table III).

The basal plasma cortisol levels on admission, as well as the levels obtained 2 and 4 hours after Piromen administration, the total white cell count, the serum albumin, haemoglobin and the % expected body weight showed no

TABLE III. DEGREE OF UNDERWEIGHT AND MEAN VALUES OF SERUM ALBUMIN, HAEMOGLOBIN AND TOTAL WHITE CELLS OF RESPONDERS AND NON-RESPONDERS

		On admission			After 5 weeks		
	% Expected body weight	Serum albumin (g/100 ml)	Haemo-globin (g/100 ml)	Total white blood cells (per mm³)	Serum albumin (g/100 ml)	Haemo-globin (g/100 ml)	Total white blood cells (per mm³)
Responders	**71,7**	**1,9**	**10,5**	**11 700**	**3,6**	**10,9**	**10 300**
Non-responders	**63,5**	**1,9**	**10,3**	**10 800**	**3,7**	**10,8**	**11 100**
Statistical difference (Mann-Whitney U-test)	**NS***	**NS***	**NS***	**NS***			

*NS = not significant ($P>0,05$).

significant correlation — in other words, the degree of malnutrition, anaemia or possible inapparent infection (as portrayed by the total white cell count), and plasma cortisol levels were not significantly interdependent.

In contrast to previous workers,[7,8] Paisey *et al.*[9] did not find high plasma cortisol levels in uncomplicated kwashiorkor. In their patients, cortisol levels were elevated only in the presence of stress situations, such as infections, hypoglycaemia, hypothermia and acidosis. Our results fully support their findings; the only very high basal plasma cortisol level (144 μg/100 ml) was found in a patient with superimposed acute pyelonephritis.

The circadian rhythm of cortisol secretion as reflected by the levels at 0800, 1600 and 2200 did not differ appreciably at the 3 different intervals from admission to clinical recovery.

CONCLUSION

The basal plasma cortisol levels and the response to Piromen stress in acute kwashiorkor were not significantly different from the corresponding values after clinical recovery. There were fewer responders one week after admission than either at the beginning or at the end, the reaction appearing somewhat delayed and blunted at this stage.

Plasma cortisol levels could not be related to the degree of body weight deficit, haemoglobin concentration, serum albumin reduction or total number of white blood cells. The hypothalamo-pituitary-adrenal interrelationship does not appear to be particularly disturbed in uncomplicated kwashiorkor.

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