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ADAPTATION TO PROTEIN DEFICIENCY: CORTISOL, THYROXINE, INSULIN AND GLUCOSE IN YOUNG PIGS

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Nutritional deficiencies place stress on the body. To maintain metabolic integrity, the body adapts by retarding or even stopping growth. In this adaptation, endocrine mechanisms such as adrenocorticol activity (Selye, 1956; Catt, 1970), thyroid function (Post, 1963; Fuller, 1969) and insulin secretion (Cahill, Herrara, Morgan, Soeldner, Steinke, Levy, Reichard & Kipnis, 1966) have been implicated. However, the role of these endocrine mechanisms in metabolic adaptation is still unresolved. Some workers maintain that the increase in plasma cortisol during malnutrition is of vital importance in maintaining metabolic integrity in malnourished children (Cassellanos & Arroyave, 1961; Lunn, Whitehead, Hay & Baker, 1973; Rao, 1974). Other workers again suggest that the rise in cortisol is merely a result of the stress of malnutrition (Abbassy, Mikhail, Zeitoun & Ragab, 1967a; 1967b; Van der Westhuysen, Jones, Van Niekerk & Belonje, 1975). Similarly decreases in both plasma thyroxine and insulin have been suggested as adaptive measures during protein deficiencies in growing children (Beas, Monckeberg& Horwitz, 1966; Singh, Anderson & Turner, 1971; Milner, 1972; Lunn *et al.*, 1973, Cahill *et al.*, 1973). In this experiment we attempted to resolve the question whether changes in the levels of these hormones are associated with either the metabolic adaptation of growth retardation or result from the stress of malnutrition. The pig was used as an experimental model and the changes in plasma cortisol, insulin, thyroxine and blood glucose during severe protein deficiency were studied.

Fifteen male piglets from three litters were weaned at a bodymass of 3.0 ± 0,2 kg (7 to 10 d old) Five of these pigs (controls) then received a dried skimmed milk powder based pig prestarter meal containing 26% digestible protein for one month. This diet was gradually substituted by a pig creep meal containing 20% digestible protein. On the other hand, the 10 experimental pigs were weaned onto and maintained on a low protein diet (5% digestible protein) which was based on haricot beans, whole wheat flour and maize starch (Platt & Steward, 1967). At two weekly intervals the bodymass of the pigs was determined and blood was sampled by cardiac puncture. Plasma glucose was determined without delay (Werner, Rey & Wielinger, 1970) and the remaining plasma was stored at −20°C for further analyses. The experiment continued for 10 weeks after the animals had been placed on their respective diets.

Plasma albumin concentration was determined by selective dye binding (Doumas, Watson & Biggs, 1972). Cortisol and thyroxine were assayed by competitive protein binding isotope dilution (Leclerq, Copinschi & Frankson, 1969; Braverman, Vaginakis, Foster & Ingbar, 1971). Insulin was determined by radioimmuno assay (Hales & Randle, 1963) using human antibody. Plasma T_3 uptake was determined by the method of Walther (1970). Multiplication of the total T_4 with its appropriate T_3 uptake gave the free thyroxine index (Anderson, 1968). Differences between medians were tested by the Willcoxon two sample test.

Over the ten week experimental period, the animals on the protein deficient diets increased their bodymasses by a median of only 1,5 kg cf. 32,5 kg for the controls (Table 1) ($P < 0,01$). Plasma cortisol concentrations did not differ between these two groups by the sixth week of malnutrition. However, only by the sixth week did the high cortisol levels found at weaning drop to a "normal" level. Between the sixth and tenth weeks of malnutrition plasma cortisol concentration increased in the malnourished pigs ($P < 0,05$) (Table 1, Figure 1). However, this increase only occurred in pigs so severely effected by malnutrition that preagonal symptoms such as lethargy and apathy had occurred (Table 2). In the case of plasma glucose there was a significant ($P < 0,01$) decrease in the lethargic malnourished pigs which occurred between the sixth and tenth weeks.

Insulin and thyroxine (both total thyroxine and free thyroxine index) changed soon after the onset of malnutrition (Figure 1). After 28 d of malnutrition plasma concentrations of insulin and thyroxine and the free thyroxine index were significantly lower ($P < 0,01$) than the control values. However, these values did not differ between alert and lethargic malnourished pigs (Table 2). The non-collagen protein content of the muscles of

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Table 1

Changes in Bodymass (kg), cortisol ($\mu g.l^{-1}$), insulin ($U.l^{-1}$), thyroxine ($\mu g.dl^{-1}$), glucose ($mg.dl^{-1}$) and albumin ($g.dl^{-1}$) concentrations in plasma and muscle non collagen protein content in pigs on protein deficient and control diets for 10 weeks

	Malnourished		Controls		Significance
	Median	Range	Median	Range	(P)
Bodymass	4,5	3,9 – 5,5	35	34 – 37	< 0,01
Cortisol	42	13 – 235	3	2 – 29	< 0,05
Insulin	9	6 – 14	22	15 – 32	< 0,01
Thyroxine	1,5	0,6 – 2,9	3,3	2,9 – 4,3	< 0,01
Free Thyroxine index	104	42 – 159	360	255 – 391	< 0,01
Plasma glucose	83	33 – 90	90	77 – 92	NS
Plasma Albumin	1,4	1,1 – 1,85	4,0	3,3 – 4,3	< 0,01
Muscle Non Collagen protein g/g Dry mass	0,51	0,38 – 0,58	0,55	0,54 – 0,58	NS

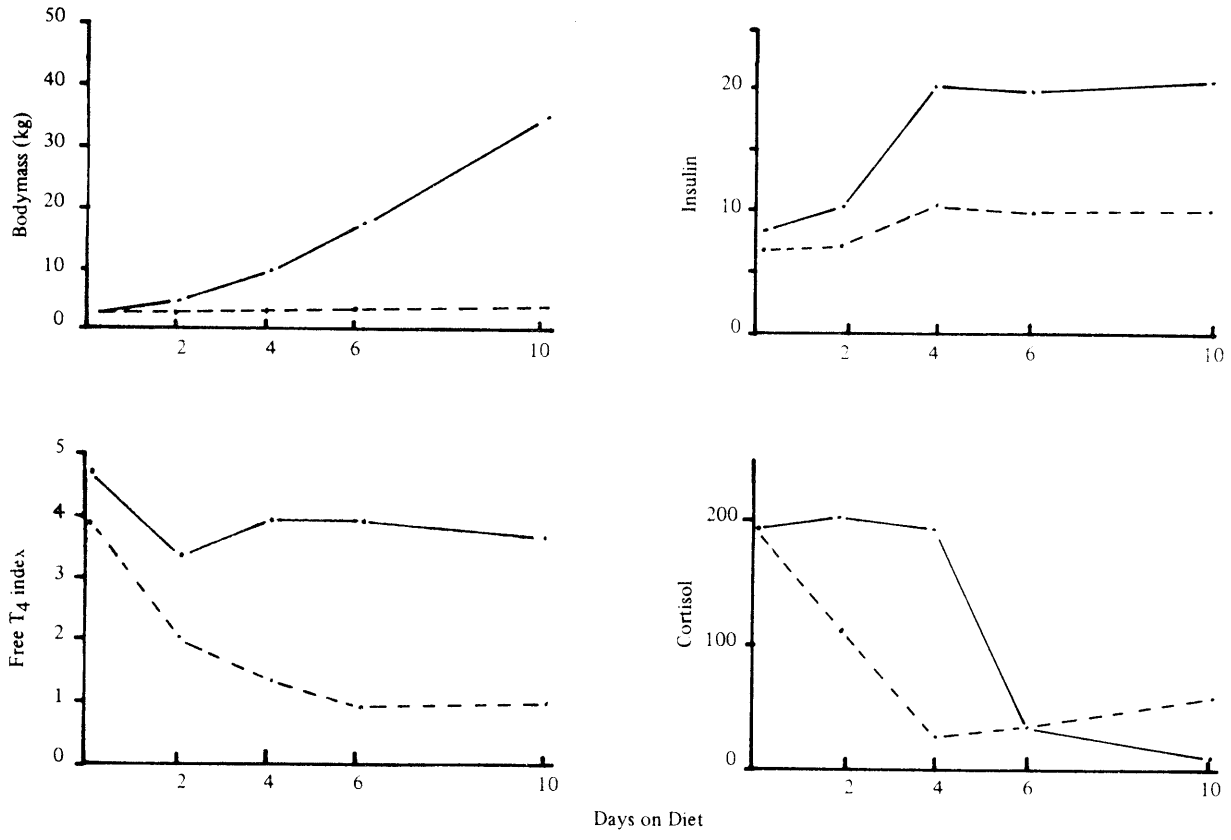

Fig. 1 *Changes in Bodymass (kg), plasma insulin ($U.l^{-1}$), free thyroxine index and Cortisol ($\mu g.l^{-1}$) in pigs fed high protein (. . . .) or low protein (– –) diets for ten weeks (Medians)*

Table 2

Bodymass and plasma concentrations of cortisol ($\mu g.l^{-1}$), glucose ($mg.dl^{-1}$), and insulin ($U.l^{-1}$), albumin ($g.dl^{-1}$), thyroxine ($\mu g.dl^{-1}$) and Free thyroxine index and non collagen protein (percentage/g of dry muscle) in 5 control, 6 malnourished but alert pigs and 4 malnourished lethargic pigs after 10 weeks on the respective diets (medians and range in parentheses)

	Control (C)	Malnourished (M)	Lethargic (L)	Probability (P)	
				C vs M + L	M vs L
Bodymass	35 (34 – 47)	4,6 (4,2 – 5,5)	4,3 (3,9 – 4,6)	< 0,01	N.S.
Cortisol	3 (2 – 29)	4 (3 – 25)	143 (81 – 125)	< 0,05	< 0,01
Insulin	22 (15 – 32)	9 (6 – 14)	9 (8 – 14)	< 0,01	N.S.
Thyroxine	3,3 (2,9 – 4,3)	1.6 (0,6 – 2,0)	1,5 (0,6 – 2,9)	< 0,01	N.S.
Free thyroxine index	360 (255 – 391)	116 (74 – 159)	86 (42 – 159)	< 0,01	N.S.
Glucose	90 (79 – 92)	82 (78 – 90)	45 (33 – 54)	N.S.	< 0,01
Albumin	4,0 (3,3 – 4,3)	1,4 (1,1 – 1,5)	1,5 (1,4 – 1,8)	< 0,01	N.S.
Non collagen protein	55 (54 – 58)	51 (44 – 58)	52 (37 – 58)	N.S.	N.S.

malnourished pigs did not differ from the control pigs (Table 1).

In farm animals, the adrenal cortex influences growth rate (Hafs, Purchas & Pearson, 1971, Van der Westhuysen, 1973) and the general tolerance to stressful conditions (Judge, Briskey, Cassens, Forrest & Meyer, 1968). In addition, thyroid function has been related to growth rate (Post, 1963) and metabolic adaptation (Fuller, 1969). However, evidence from the present study indicates that a retardation of growth rate as a result of protein deficiency does not effect plasma cortisol significantly. This experiment appears to confirm previous work on young growing children (Van der Westhuysen, 1975) that the role of cortisol in adaptation to malnutrition is insignificant. So for instance in this study, plasma cortisol concentration increased slightly after six weeks of malnutrition and then only after a decrease in plasma glucose. Further analyses indicated that no increase occurred in the cortisol levels of alert malnourished pigs but there were very high levels of cortisol in severely affected preagonal lethargic malnourished pigs. This suggestes that malnutrition *per se* does not result in increased plasma cortisol levels.

The plasma glucose levels are noteworthy. Once again there was no difference in these levels between the control and alert malnourished animals. On the other hand, the average plasma glucose level in the lethargic malnourished pigs was much lower than in the other two groups and it is conceivable that this low glucose level stimulated the cortisol increase in these animals.

Insulin was found to be low during malnutrition. This is similar to findings in malnutrition in children (Milner, 1972). However, the reason why the alert malnourished piglets had normal plasma glucose levels while the levels in lethargic pregnant pigs was much lower cannot be explained on the basis of the low insulin or high cortisol levels found in these animals. This situation points to a failure in carbohydrate metabolism.

Thyroid function decreased significantly in the malnourished groups. However, the insignificant difference between the levels in the successfully adapted alert malnourished group and the maladapted lethargic group casts doubt on the significance of the thyroid gland in the maintenance of metabolic integrity during protein malnutrition.

Therefore, although this study indicates that protein synthesis and growth rate are retarded during protein deficiency, the successful maintenance of metabolism in growth retarded pigs does not depend primarily on the hormones which were investigated.

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