4. Glaubitt, D. M. H., Schülter, J. H. and Haberland, K. V. R. (1975): J. nucl. Med., **16**, 769.
5. Kniseley, R. M. (1972): Sem. nucl. Med., **2**, 71.
6. Merrick, M. V., Smith, E. C. G., Lavendar, J. P. and Szur, L. (1975): J. nucl. Med., **16**, 66.
7. Chaudhuri, T. K., Ehrahrdt, L. D. de G. and Christie, J. H. (1974): *Ibid.*, **15**, 667.
8. Beck, R. N. (1964): *IAEA Symposium on Medical Radio-isotope Scanning*, vol. 1. p. 211. Vienna: IAEA.
9. Newell, R. R., Saunder, W. and Miller, W. (1952): Nucleonics, **10**, 36.
10. Beck, R. N. (1961): J. nucl. Med., **2**, 314.
11. Finch, C. A., Deubelbeiss, K., Cook, J. D., Eschbach, J. W., Harker, L. A., Funk, D. D., Marsaglia, G., Hillman, R. S., Slichter, S., Adamson, J. W., Ganzoni, A. and Giblett, E. R. (1970): Medicine, **49**, 17.
12. Cavill, I. (1971): J. clin. Path., **24**, 472.
13. Linman, J. W. and Saarni, M. J. (1974): Semin. Haemat., **9**, 93.

Nutrition Research

The Effect of Protein Energy Malnutrition on Plasma Renin and Oedema in the Pig

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SUMMARY

Five litter-mate male pigs, aged 7 days and fed a standard Pig Industry Board diet containing 190 g/kg dry mass of digestible protein, were compared with 10 male pigs from two litters fed a protein-deficient diet (50 g/kg) for a period of 70 days. The 10 experimental animals developed oedema between the 42nd and 70th days of the study and 4 of them became lethargic. Although the 10 experimental animals showed the typical biochemical changes characteristic of protein energy malnutrition (PEM), including changes in muscle electrolytes, liver fat and plasma albumin, the 4 lethargic animals showed a significant increase in effective plasma renin activity (EPRA) only by the 70th day of the study. Since oedema preceded any increase in EPRA in some pigs and developed in others without any change in EPRA, it is suggested that the increased renin activity is not responsible for the initial fluid retention and oedema.

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Previous work on children[9,22] and experimental animals[20,21,24] suggests that the development of oedema during protein energy malnutrition (PEM) may be the result of increased activity of the renin-angiotensin system. The increased renin activity may explain the increased plasma aldosterone,[11] decreased glomerular filtration rate,[1] and the consequent retention of sodium and water[6] found in patients with kwashiorkor. However, it has not been established whether this increased renin is a primary cause of water retention and consequent oedema, or whether the increase is due to other changes which occur during PEM.[22] Therefore, an experiment was designed to examine the time relationship between the onset of oedema and the increase in plasma renin activity, using the pig as the experimental model.

MATERIALS AND METHODS

Fifteen male pigs from 3 litters, aged 7 days (3,0 ± 0,2 kg), were studied over a period of 70 days. The pigs were assigned at random to two groups: a control group of 5 pigs fed a standard Pig Industry Board diet containing 190 g/kg dry mass digestible protein, and an experimental group of 10 pigs fed a protein-deficient diet based on whole-wheat flour and maize starch and containing 50 g/kg digestible protein.[15] Both groups received antibiotics, and mineral and vitamin supplements.

The pigs were examined daily for lethargy and oedema, which was first observed in the neck and at the base of the tail. On the 1st, 14th, 28th, 42nd and 70th days the glomerular filtration rate was determined by using ^{51}C-

EDTA[2] under chlorpromazine sedation (3 mg/kg body mass) and a 10 ml blood sample was collected, by cardiac puncture, into an ice-cold plastic syringe containing EDTA. The blood was kept on crushed ice before being centrifuged and the plasma was stored at −20°C. On the 70th day, after bromsulphthalein retention[17] had been determined, the pigs were killed with pentobarbitone. Effective plasma renin activity (EPRA) was bio-assayed after acid incubation and fuller's earth extraction as described.[9,20,22] The coefficient of variation of the determination was 9,9%.[22] Aldosterone was determined by radio-immunoassay (Biokits; Biolab, Belgium) after methylene chloride extraction[13] of the plasma, and separation on precoated silica gel plates (Merck, Darmstadt) using an ethanol-benzene (10:90) solvent. The recovery of tritiated aldosterone from plasma was 24 - 27%. Albumin,[4] urea,[26] aminotransferase,[16] sodium (flame photometry),[26] potassium (flame photometry),[26] magnesium (atomic absorption)[23] and non-collagen protein[10] were determined by standard methods on plasma and on muscle after dry-ashing. The percentage of water was determined by freeze-drying and the liver fat was estimated by ether extraction after acid hydrolysis. The significance of the difference between groups was determined by Wilcoxon's method.

RESULTS

Table I shows the difference in water and mineral contents of the skin and muscle, the non-collagenous protein content of muscle and the liver fat content of the experimental and control groups. There was no difference in the bromsulphthalein retention of the 2 groups (4,8% in 30 min). Table II shows the change in plasma albumin, potassium, sodium and aminotransferase in the experimental and control animals during the 70-day experimental period. There was no change in the plasma creatinine concentrations. Table III shows the changes that occurred between the 1st and 70th day of the study. Four pigs in the control group became oedematous and lethargic and 6 pigs became oedematous but remained alert during the 70 days. Although no significant changes occurred in the aldosterone, glomerular filtration rate or plasma urea of the experimental pigs, the 4 lethargic pigs showed significant changes in EPRA (Table III). These changes also include the time of onset of oedema. Whereas plasma albumin fell to its lowest concentration at least 14 days *before* the appearance of oedema, the changes that occurred in renin activity invariably *followed* the onset of oedema.

TABLE I. PERCENTAGE OF WATER IN MUSCLE, AND IN COMBINED SKIN AND SUBCUTANEOUS TISSUE, THE WET-MUSCLE SODIUM, POTASSIUM AND MAGNESIUM (mmol/kg WET MASS), MUSCLE NON-COLLAGENOUS PROTEIN (% WET MASS) AND LIVER FAT (% WET MASS) IN THE CONTROL GROUP OF 5 PIGS AND THE EXPERIMENTAL GROUP OF 10 PIGS

	Control		Experimental		
	Median	Range	Median	Range	Probability
Skin water	33	26 - 36	78	69 - 86	<0,01
Muscle water	74	73 - 75	83	80 - 89	<0,01
Muscle sodium	25	22 - 26	47	41 - 58	<0,01
Muscle potassium	70	63 - 73	22	14 - 34	<0,01
Muscle magnesium	15	14 - 16	7	4 - 19	NS
Non-collagenous protein	15	15 - 16	8	7 - 9	<0,01
Liver fat	1,5	0,8 - 2,8	11,0	4,0 - 19,3	<0,01

DISCUSSION

Protein energy malnutrition in the pig produced the expected changes, which include: a failure of growth,[25] retention of water in the muscle and subcutaneous tissue,[18] a decrease in muscle potassium,[12] magnesium[14] and non-collagenous protein concentrations,[6] an increase in liver fat,[5] an increase in serum transaminases,[8] a decrease in plasma potassium concentration,[12] and a decrease in plasma albumin.[3,7]

All the experimental animals developed oedema between the 6th and 10th weeks of the study. Six pigs remained active and alert while the other 4 became progressively lethargic until they collapsed. Although all the

TABLE II. BODY MASS (kg), PLASMA ALBUMIN (g/dl), POTASSIUM (mmol/l), SODIUM (mmol/l), SERUM AMINOTRANSFERASE (UNITS) IN THE CONTROL GROUP OF 5 PIGS AND IN THE EXPERIMENTAL GROUP OF 10 PIGS

	Control		Experimental		
	Median	Range	Median	Range	Probability
Body mass	35,5	34 - 47	4,60	3,9 - 5,5	<0,01
Change of mass	+ 32,3	+ 30,5 - 42,5	+ 1,0	+ 1,0 - 1,5	<0,01
Albumin	3,8	3,3 - 4,3	1,3	1,0 - 2,1	<0,01
Change in albumin	+ 1,2	+ 0,2 - 1,6	− 1,6	− 1,0 - − 2,1	<0,01
Plasma potassium	7	6 - 7	5	4,1 - 6,1	<0,01
Change in potassium	− 2	+ 1 - − 3	− 0,5	− 2,5 - + 0,8	<0,1
Plasma sodium	155	148 - 168	142	133 - 150	<0,01
Change in sodium	+ 15	+ 2 - + 30	+ 6	−12 - + 15	<0,01
Aminotransferase	8	5 - 10	14	9 - 20	<0,01
Change in aminotransferase	+ 2	0 - + 6	+ 6	+ 2 - + 16	<0,01

TABLE III. ONSET OF OEDEMA (WKS), PLASMA RENIN ACTIVITY (ng/ml/h), PLASMA ALDOSTERONE (μg/dl), GLOMERULAR FILTRATION RATE (ml/min/kg^{0,75}), AND UREA (mg/dl) AND THE CHANGES THAT OCCURRED BETWEEN THE 1ST AND THE 70TH DAY OF THE STUDY IN 5 PIGS IN THE CONTROL GROUP (C), IN 4 PIGS THAT BECAME OEDEMATOUS AND LETHARGIC (L) AND IN 6 PIGS THAT BECAME OEDEMATOUS BUT REMAINED ALERT (O)

	Control (C)		Oedema (O)		Lethargy (L)		Probability	
	Median	Range	Mean	Range	Median	Range	C v. O + L	O v. L
Onset of oedema	Nil	—	10	8 - 10	6	4 - 10		
Renin activity	4	2 - 7	3	3 - 26	50	50 - 107	<0,01	<0,01
Change in renin	+ 3	+ 2 - + 4	0	−12 - +23	+ 52	46 - 102	<0,01	<0,01
Aldosterone	3	2,6 - 3,8	4	3 - 9	7	5 - 12	NS	NS
Change in aldosterone	+ 2	− 1 - + 4,5	+ 3	1 - 6	+ 5	2 - 9	NS	NS
Glomerular filtration rate (GFR)	3,3	3,1 - 3,4	0,9	0,8 - 3,0	0,8	0,7 - 3,0	NS	NS
Change in GFR	+ 1,0	0,5 - 2,1	− 0,6	1,5 - 0,7	− 0,6	−1,6 - 0,7	NS	NS
Urea	23	22 - 27	20	8 - 24	33	12 - 51	NS	NS
Change in urea	− 2	0 - − 7		+ 1 - − 12	23	+ 1 - 38	NS	NS

experimental animals developed oedema, the EPRA increased in the 4 lethargic pigs only, and then only after oedema had developed. This corroborates previous findings in children with kwashiorkor or marasmus in whom oedema was not necessarily accompanied by an increased EPRA, or vice versa,[2] but increased markedly in fatal cases. Our findings suggest that the renin-angiotensin system is not responsible for the initial fluid retention and the development of oedema in PEM, but that the increase in EPRA is a secondary response to a terminal change in cardiovascular function.[19,27]

REFERENCES

1. Alleyne, G. A. D. (1967): Pediatrics, **39**, 400.
2. Chantler, C., Garnett, E. S., Parsons, V. and Veale, N. (1969): Clin. Sci., **37**, 169.
3. Coward, W. A., Whitehead, R. G. and Coward, Dorothy G. (1972): Brit. J. Nutr., **28**, 433.
4. Doumas, B. J., Watson, W. A. and Biggs, H. G. (1971): Clin. chim. Acta, **31**, 87.
5. Garrow, J. S., Fletcher, K. and Halliday, D. (1965): J. clin. Invest., **44**, 417.
6. Garrow, J. S., Smith, R. and Ward, E. E. (1968): *Electrolyte Metabolism in Severe Infantile Malnutrition.* Oxford: Pergamon Press.
7. Grimble, R. E. and Whitehead, R. G. (1972): Brit. J. Nutr., **23**, 791.
8. Kinnear, A. A. and Pretorius, P. J. (1956): Brit. J. Med., **1**, 528.
9. Kritzinger, E. E., Kanengoni, E. and Jones, J. J. (1972): Lancet, **1**, 412.
10. Lowry, O. H., Rosenbrough, N. J., Farr, A. C. and Randall, R. J. (1951): J. Biol. Chem., 193, 265.
11. Lurie, A. D. and Jackson, W. P. U. (1962): Amer. J. clin. Nutr., **11**, 115.
12. Mann, M. D., Bowie, M. D. and Hansen, J. D. L. (1972): S. Afr. med. J., **46**, 2062.
13. Mattingly, D. (1962): J. Clin. Path., **15**, 374.
14. Montgomery, R. D. (1960): Lancet, **2**, 74.
15. Platt, B. S. and Steward, R. J. C. (1967): J. Endocr., **38**, 121.
16. Reitman, S. and Frankel, S. (1957): Amer. J. clin. Path., **28**, 56.
17. Rosenthal, S. M. and White, E. C. (1925): J. Amer. med. Ass., **84**, 1112.
18. Smith, R. (1960): Clin. Sci., **19**, 275.
19. Smythe, P. M., Swanepoel, A. and Campbell, J. A. H. (1962): Brit. med. J., **1**, 67.
20. Van der Westhuysen, J. M. and Jones, J. J. (1974): S. Afr. med. J., **48**, 2534.
21. Van der Westhuysen, J. M., Jones, J. J. and Van Niekerk, C. H. (1975): *Ibid.*, **49**, 1799.
22. Van der Westhuysen, J. M., Kanengoni, E., Jones, J. J. and Van Niekerk, C. H. (1975): *Ibid.*, **49**, 1729.
23. Varley, H. (1965): *Practical Clinical Biochemistry.* London: William Heinemann.
24. Warton, C. M. R., Kanengoni, E. and Jones, J. J. (1973): S. Afr. med. J., **47**, 1498.
25. Wellcome Working Party on Infantile Malnutrition (1970): Lancet, **2**, 302.
26. Wootton, I. D. P. (1964): *Micro-analyses in Medical Biochemistry.* London: Churchill.
27. Wharton, B. A., Howells, G. R. and McCance, R. A. (1967): Lancet, **2**, 384.

NEEDLE ASPIRATION BIOPSY

Aspiration of material for biopsy by means of a needle was performed on 130 patients with lymphadenopathy or subcutaneous nodules. Within this group there were 88 malignant specimens, with 84 interpreted as positive and 4 as suspect. There were no false-positive findings in benign specimens. The method is rapid, inexpensive and relatively atraumatic, and can be utilised instead of the usual surgical excision.

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SOCIAL SURGERY

We now live in a body-conscious and competitive society in which disfigurements may adversely affect career prospects, position and self-esteem. A large number of operations have been devised, such as nasal reduction, face-lift, and abdominal lipectomy, to correct real or imagined deformities. Two relatively new procedures are the treatment of axillary hyperhidrosis and reconstruction of the female breast after mastectomy.

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