Our results show that the prognosis of expatriate patients treated in Hong Kong and remaining there is excellent for at least two and a half years. Long-term follow-up studies in tropical sprue are rare. Hazari and Woodruff (1958) reported that 17 patients who had contracted tropical sprue in India 10 years previously and had been evacuated to Britain were all at full work, although some third of these had mild and intermittent symptoms but were not disabled by them. As more effective forms of treatment were available to our patients their outlook should be at least as good, but this point will need to be established.

Summary

Thirty patients who contracted tropical sprue in Hong Kong are described. Nine of them became ill at the beginning of the hot season with initial complaints of lassitude and anorexia without disturbance of the bowels, and the significance of these early symptoms is stressed.

Treatment with antibacterial drugs was not as effective as treatment with large doses of folic acid, but it is suggested that some patients who have been ill for more than three months may require both forms of therapy before an optimal response is obtained.

It was confirmed that folic acid usually reverses the intestinal lesion in these patients provided an adequate amount of the drug is given; a total of less than 50 mg. was generally ineffective.

Twenty-six patients remained in Hong Kong for periods of up to two and a half years after treatment, and none relapsed.

We are deeply indebted to our many medical and nursing colleagues who worked with us; to Professor A. C. Frazer, who advised on sprue research in Hong Kong and who has permitted us

to include data on four cases which were transferred to his unit in Birmingham; and to Dr. A. C. Hobson (then Lieutenant-Colonel R.A.M.C.), who handed on the sprue project in Hong Kong to one of us (J. F. W.). We are also grateful to Lieutenant-Colonels S. A. Biggart and C. B. F. Downie, R.A.M.C., who were in charge of eight of the patients investigated. Dr. B. C. Morson and Lieutenant-Colonel N. W. J. England, R.A.M.C., have been most helpful in reviewing the small-intestinal biopsy specimens, and Professor D. L. Mollin and Colonel W. O'Brien, late R.A.M.C., have given us invaluable advice and helpful criticism throughout the preparation of this paper. Finally, we would like to thank the Director-General Army Medical Services for permission to use case notes and records for this publication.

REFERENCES

- Ayrey, F. (1947). *Trans. roy. Soc. trop. Med. Hyg.*, **41**, 377.
 Crosby, W. H., and Kugler, H. W. (1957). *Amer. J. dig. Dis.*, **2**, 236.
 Dacie, J. V. (1956). *Practical Haematology*, 2nd ed. Churchill, London.
 Frazer, A. C. (1958). *Proceedings of World Congress of Gastroenterology*. Williams and Wilkins, Baltimore.
 French, J. M., Gaddie, R., and Smith, N. M. (1956). *Quart. J. Med.*, **25**, 333.
 Gardner, F. H. (1956). *Arch. intern. Med.*, **98**, 44.
 Hazari, O. K., and Woodruff, A. W. (1958). *Brit. med. J.*, **2**, 344.
 Hillary, W. (1966). *Observations on the changes of the Air and Concomitant Epidemic Diseases in the Island of Barbados*, edited by L. Hawes, W. Clarke, and R. Collins, 2nd ed. London.
 Hutner, S. H., Bach, M. K., and Ross, G. I. M. (1956). *J. Protozool.*, **3**, 101.
 Kay, A. W. (1953). *Brit. med. J.*, **2**, 77.
 Klipstein, F. A. (1964). *Gastroenterology*, **47**, 457.
 Mollin, D. L. (1961). *Trans. med. Soc. Lond.*, **78**, 51.
 O'Brien, W., and England, N. W. J. (1964). *Brit. med. J.*, **2**, 1573.
 Rosenthal, F. D. (1952). M.D. Thesis, University of London.
 Santini, R., Sheehy, T. W., and Martínez de Jesus, J. (1961). *Gastroenterology*, **40**, 772.
 Sheehy, T. W., Cohen, W. C., Wallace, D. K., and Legters, L. J. (1965). *J. Amer. med. Ass.*, **194**, 1069.
 — and Floch, M. H. (1964). *The Small Intestine: its function and diseases*. Hoeber, New York.
 Shiner, M. (1956). *Lancet*, **1**, 85.
 van de Kamer, J. H., Huinink, H. ten B., and Weyers, H. A. (1949). *J. biol. Chem.*, **177**, 347.
 Waters, A. H., and Mollin, D. L. (1961). *J. clin. Path.*, **14**, 335.
 Webb, J. F. (1956). M.D. Thesis, Dunelm.

Hypoproteinaemia in Anaphylactoid Purpura

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Anaphylactoid (Henoch-Schönlein) purpura may produce a nephrotic syndrome and thus cause hypoalbuminaemia. However, some years ago we observed a patient with this disease in whom the serum albumin level was reduced at a time when urinary losses of protein were insignificant. Evidence of liver dysfunction was absent, but gastrointestinal complications of the disease were prominent. It was therefore suspected that the hypoalbuminaemia was due to abnormal losses of protein into the bowel. We here record observations on five patients with anaphylactoid purpura which suggest that protein-losing enteropathy may complicate this disease. This association does not seem to have been reported to date (Waldmann, 1966).

Methods

Loss of protein via the gut was assessed by measuring the radioactivity present in a five-day collection of faeces after the intravenous injection of ^{131}I -labelled polyvidone (P.V.P.) or $^{51}\text{CrCl}_3$. The former was used according to the method of

Gordon (1959) with ^{131}I -P.V.P. obtained from the Radiochemical Centre, Amersham. The use of $^{51}\text{CrCl}_3$ followed the method of Rubini and Sheehy (1961).

Normal values obtained in this hospital for faecal excretion of radioactivity in these tests are given in the Table; they

Serum Albumin Levels and Associated Features of Five Patients with Anaphylactoid Purpura

Case No.	Sex and Age	Serum Albumin (g./100 ml.)	Proteinuria*	Gastro-intestinal Symptoms				Faecal Excretion (% of dose)	
				Vomiting	Colic	Diarrhoea	Bleeding	^{131}I -P.V.P.	$^{51}\text{CrCl}_3$
1	M 39	2.8	0-Tr.	—	+	+	+	11.9	
2	M 49	3.7	++ + +	—	—	—	—	0.5	
3	F 58	2.5	0-Tr.	+	+	+	+		4.3
4	M 60	3.7	0.2-9†	+	+	+	+		1.3
5	F 32	4.6	Tr.	—	+	—	—		2.4
Highest value in 7 control subjects				..	..	..	..	0.26	
" " " " "				..	..	..	..		0.28

* Tr. = Trace with salicylsulphonic acid.

† g. protein/day.

‡ No gastro-intestinal bleeding occurred during the ^{131}I -P.V.P. test.

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agree with those reported by other workers (Gordon, 1959 ; Schwartz and Jarnum, 1959 ; Rubini and Sheehy, 1961 ; Rubini *et al.*, 1961). These methods provide only approximate estimates of protein loss into the gut ; their validity and limitations are discussed below.

Case 1

A 39-year-old man was admitted to hospital in 1962. During the previous week he had developed a rash on the legs, diarrhoea, and central abdominal colic. His ankles, right knee, and elbows had become swollen and painful. He showed the characteristic skin eruption of anaphylactoid purpura with raised purpuric lesions, many of which had a surrounding area of erythema. These lesions were prominent on the buttocks, feet, and forearms. Small effusions were present in some of the painful joints. Central abdominal tenderness and increased bowel sounds were noted and the stool contained blood. No abnormalities were detected in the heart or lungs, and the blood-pressure was 140/70. He gave no history of recent infection and had not recently taken any drugs.

Examination of his blood gave these results: haemoglobin 13.9 g./100 ml. ; white blood cells 16,800/c.mm. ; platelets 357,000/c.mm. ; serum antistreptolysin O titre <50 units/ml. ; serum albumin 3.2 and serum globulin 0.9 g./100 ml., with reduction of the γ -globulin on electrophoresis. Subsequent values for the serum albumin are shown in the Chart ; serum globulin levels became normal within three weeks.

On the patient's admission the jugular venous pressure was not raised and there was no oedema, but he subsequently developed transient signs of an expanded extracellular-fluid volume with raised venous pressure and oedema. Daily urine volumes were less than 1 litre at this time, but the highest blood urea level recorded was 45 mg./100 ml. The heart sounds and the electrocardiogram remained normal. This episode of fluid retention lasted for three days, and spontaneous diuresis then occurred.

Urine tested on admission gave a faint cloudiness with salicyl-sulphonic acid, but the deposit was normal. Twenty-four-hour collections of urine were tested daily with salicylsulphonic acid, the results, classified in the conventional way by the same observer, being shown in the Chart. On the seventh day urinary protein excretion was less than 250 mg./day. Thereafter the excretion of urinary protein increased considerably (see Chart), and hyaline and granular casts appeared in the urinary deposit.

For a week after admission the patient had diarrhoea with considerable abdominal colic and distension. On his admission the stools were blood-stained, but throughout the ^{131}I -P.V.P. study daily tests for occult blood were negative. X-ray examination showed fluid levels and an excess of intestinal gas. The serum albumin level was reduced and faecal excretion of radioactivity after intravenous ^{131}I -P.V.P. was abnormally high at this time (see Table and Chart), whereas faecal fat excretion was normal, 2.4 g./day.

Three weeks later the ^{131}I -P.V.P. test was repeated with a normal result (Table and Chart). At this time abdominal symptoms and signs were absent and the rash and arthritis had disappeared. The serum albumin level had become normal, although proteinuria persisted (see Chart). The patient eventually made a complete recovery.

Comment.—This patient developed anaphylactoid purpura with involvement of the gastrointestinal tract. The episode of fluid retention was presumably due to the acute nephritis which may complicate this disease. Proteinuria with an abnormal urinary sediment occurred, although the blood urea rose only slightly. The serum albumin was reduced and the faecal excretion of ^{131}I -P.V.P. greatly increased early in the disease, at a time when proteinuria was minimal (see Chart). Later in the illness, when proteinuria was much greater, both serum albumin and ^{131}I -P.V.P. excretion were normal.

Cases 2-5

These patients had the characteristic rash of anaphylactoid purpura with normal platelet counts. In Cases 1-3 hypoalbuminaemia was present and gastrointestinal disturbances were prominent (see Table). At the time when hypoalbuminaemia was discovered melaena had not been severe enough to warrant blood transfusion in any patient, but one (Case 2) was transfused later in his illness.

No isotope studies were performed in Case 2, which is reported because the reduction in serum albumin level found was not ascribable to proteinuria. Tests for protein were negative on most specimens of urine examined, although an occasional trace was detected. The urinary sediment was normal. Serum albumin concentrations of 2.5 and 2.6 g./100 ml. were recorded.

In Case 3 the gastrointestinal tract was severely affected and the patient was admitted in a state of dehydration. Her blood urea was then 162 mg./100 ml., but it fell to 34 mg./100 ml. after four days of intensive fluid therapy. However, proteinuria persisted throughout the illness, the highest daily output recorded being 2.9 g. The urine also contained hyaline casts, and it is possible that the patient had nephritis. The serum albumin fell to 2.5 g./100 ml. but later rose to 4.0 g./100 ml. This rise occurred after the gastrointestinal symptoms had abated, but when the proteinuria was as heavy as previously. Tests of liver function were normal on two occasions.

Cases 4 and 5 had mild forms of the disease: serum albumin levels were normal and gastrointestinal symptoms were limited to colic. However, an increased amount of radioactivity was recovered from the faeces in Case 5 after intravenous injection of $^{51}\text{CrCl}_3$ (see Table).

Discussion

The hypoalbuminaemia which developed in Cases 1-3 cannot be attributed to urinary protein losses. Albuminuria was trivial and intermittent in Cases 1 and 2 when the serum albumin level was reduced, but appreciable albuminuria developed later in Case 1, when the serum albumin level was normal (see Chart). Albuminuria was present throughout the illness in Case 3, but the highest value obtained for urinary protein excretion was 2.9 g./day. Moreover, the serum albumin level returned to normal in Case 3 when the gastrointestinal symptoms abated, although proteinuria was at least as heavy at this time.

The increased faecal excretion of the plasma protein isotopic markers indicates that protein losses via the gut were excessive. It should be realized that these isotope tests provide only an approximate measure of gastrointestinal protein loss. Since these tests were introduced (Gordon, 1959 ; Rubini *et al.*, 1961) various refinements have been attempted (Jeejeebhoy and Coghill, 1961 ; Jones and Morgan, 1963). However, the problems attendant on these more complicated procedures have not wholly been resolved (Freeman, 1964, and following discussion ; Waldmann, 1966). The techniques used in this study may not provide an accurate quantitative measurement of gastrointestinal protein loss, but, as normal subjects excrete so little radioactivity in the faeces in such tests, it seems reasonable to

conclude that there was an increased protein exudation into the bowel in Cases 1 and 3 (see Table).¹

The normal values for faecal excretion of ¹³¹I and ⁵¹Cr quoted in the Table agree with those reported by Gordon (1959) and Schwartz and Jarnum (1959) for ¹³¹I-P.V.P. and by Rubini and Sheehy (1961) and Rubini *et al.* (1961) for ⁵¹CrCl₃. However, in the former two reports faecal recovery of ¹³¹I-P.V.P. in control subjects was occasionally as high as 1.5% and 1.03% respectively, while in the study by Rubini and Sheehy (1961) faecal recovery of ⁵¹Cr was up to 1%. The excretion of 1.3% of the injected isotope in Case 4 cannot therefore be regarded as abnormal. However, the excretion of 2.4% of the administered dose in Case 5 may well be abnormally high, although the serum albumin level was normal. In this patient albumin production had presumably increased enough to prevent hypoalbuminaemia, as in some of the patients studied by Jeejeebhoy (1964).

It is very unlikely that loss of blood into the bowel entirely accounted for the recovery of isotope in the faeces. Bleeding did not occur in Case 1 during the ¹³¹I-P.V.P. test, daily tests for occult blood in the stools being consistently negative. Hypoalbuminaemia was present in Case 2 before gastrointestinal bleeding was detected. No bleeding occurred in Case 5 but the faecal recovery of isotope was elevated. Moreover, far larger haemorrhages due to diseases such as peptic ulcer do not usually produce hypoalbuminaemia.

Although these results indicate that protein-losing enteropathy contributed to the hypoalbuminaemia in Cases 1–3, two other possible factors have not been excluded. Albumin production may have been reduced in these patients. None had clinical evidence of liver disease, and liver-function tests in Case 3 gave normal results. Jeejeebhoy (1964) has suggested that in certain gastrointestinal diseases excessive faecal losses of nitrogen may eventually limit albumin synthesis. It seems unlikely that this mechanism was important in these patients, whose gastrointestinal disturbances were of short duration before hypoalbuminaemia was detected. Finally, it is conceiv-

able that an abnormal distribution of albumin between the intravascular and extravascular compartments was present, as described by Weinbren *et al.* (1965), in one patient with systemic lupus erythematosus.

The fact that gastrointestinal symptoms were most marked in those patients with hypoalbuminaemia (see Table) lends support to the view that this deficiency was due to abnormal protein losses into the gut. Such losses are presumably associated with the gut lesions described in anaphylactoid purpura, which include thickening of the bowel wall with localized or extensive haemorrhages (Bailey, 1930; Bywaters *et al.*, 1957). It is of interest to note that in five of the cases described by Bywaters *et al.* (1957) oedema was the presenting symptom, whereas only two patients had signs of renal involvement at the onset of the disease, and both these had previously suffered from nephritis. It seems possible that when oedema antedated renal disease in the latter series hypoalbuminaemia due to protein-losing enteropathy was the cause.

Summary

Hypoalbuminaemia may occur in anaphylactoid purpura when urinary protein losses are trivial.

Evidence is presented to suggest that excessive protein losses into the gut may contribute to the hypoalbuminaemia.

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REFERENCES

- Bailey, H. (1930). *Brit. J. Surg.*, **18**, 234.
Bywaters, E. G. L., Isdale, I., and Kempton, J. J. (1957). *Quart. J. Med.*, **26**, 161.
Freeman, T. (1964). In *The Role of the Gastrointestinal Tract in Protein Metabolism*, edited by H. N. Munro, p. 125. Blackwell, Oxford.
Gordon, R. S. (1959). *Lancet*, **1**, 325.
Jeejeebhoy, K. N. (1964). In *The Role of the Gastrointestinal Tract in Protein Metabolism*, edited by H. N. Munro, p. 357. Blackwell, Oxford.
— and Coghill, N. F. (1961). *Gut*, **2**, 123.
Jones, J. H., and Morgan, D. B. (1963). *Lancet*, **1**, 626.
Rubini, M. E., and Sheehy, T. W. (1961). *J. Lab. clin. Med.*, **58**, 892.
— Meroney, W. H., and Louro, J. (1961). *Ibid.*, **58**, 902.
Schwartz, M., and Jarnum, S. (1959). *Lancet*, **1**, 327.
Waldmann, T. A. (1966). *Gastroenterology*, **50**, 422.
Weinbren, I., Taggart, P. I., and Glass, H. I. (1965). *Lancet*, **1**, 512.

¹ The validity of ⁵¹CrCl₃ and ¹³¹I-P.V.P. in the qualitative assessment of gastrointestinal protein loss is further supported by a recent study (Roorwelt, K., *Scand. J. clin. Lab. Invest.*, 1966, **18**, 405).

Non-tumoral Stenosis of the Aqueduct in Adults

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Though non-tumoral stenosis of the aqueduct has long been described as a common cause of hydrocephalus in infants and young children, its occurrence in adults has been recorded infrequently. In childhood the general picture of the clinical features (Dandy, 1920, 1945; Pennybacker, 1940; Torkildsen, 1947, 1948, 1960) is of an infant or child whose head is steadily enlarging from hydrocephalus, who is overweight and usually slow at school, and who has developed increasing headache with slight clumsiness of movements, together with a low-grade papilloedema. Plain x-ray films of the skull show, in addition to enlargement of the skull vault, pressure changes in the dorsum sellae and a shallow posterior fossa. The diagnosis is confirmed by ventriculography with or without lumbar encephalography. Cases of aqueduct stenosis in adults have been described (Spiller and Allen, 1907; Petit-Dutaillis *et al.*,

1950; Paine and McKissock, 1955). These authors, however, did not delineate any specific syndromes or patterns of symptom-presentation in adults. Our own findings suggest that certain patterns do occur which are variants of the presentation of chronic hydrocephalus in adults from other causes. Among these patterns are the presentation of impaired memory, of epilepsy, of unsteady gait, of headaches and other features of increased intracranial tension, and of endocrine disorders and features indicative of hypothalamic involvement. Below we report a series of 10 cases in patients over the age of 25 years, in whom this lesion seemed responsible for symptoms.

The Patients

The salient features of our 10 cases are listed in Table 1. In only two (Cases 9 and 10) did the symptoms date from childhood. The duration of symptoms varied from 1 to 39

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