these experimental results. Some information can be gained by using a chart of the Hynes-Whitby type.

Our thanks are due to Dr. A. H. T. Robb-Smith, Director of Pathology, Radcliffe Infirmary, Oxford; to Dr. R. G. Macfarlane, in whose department this investigation was carried out, for suggesting the problem; to Dr. Macfarlane and Dr. Rosemary Biggs for constant advice and encouragement during the experiments; to Dr. O. G. Dodge for help in some of the experimental work; and to the donors of our normal blood specimens.

REFERENCES

- Bendien, W. M., Neuberger, J., and Snapper, I. (1932). *Biochem. Z.*, 247, 306.
 Best, W. R. (1950). *Amer. J. Clin. Path.*, 20, 87.
 Bönniger, M., and Hermann, W. (1923). *Klin. Wschr.*, 2, 744.
 Bouton, S. M., jun. (1938). *J. Lab. clin. Med.*, 23, 519.
 Bunting, H. (1939). *Amer. J. med. Sci.*, 198, 191.
 Cutler, J. W., Park, F. R., and Herr, B. S. (1938). *Amer. J. med. Sci.*, 195, 734.
 Fahraeus, R. (1921). *Acta med. scand.*, 55, 1.
 — (1929). *Physiol. Rev.*, 9, 241.
 Gram, H. C. (1928). *Acta med. scand.*, 68, 108.
 — (1929). *Ibid.*, 70, 242.
 Ham, T. H., and Curtis, F. C. (1938). *Medicine*, 17, 447.
 Hambleton, A., and Christianson, R. A. (1939). *Amer. J. med. Sci.*, 198, 177.
 Hynes, M., and Whitby, L. E. H. (1938). *Lancet*, 2, 249.
 Newham, H. B., and Martin, P. H. (1928). *Quart. J. Med.*, 22, 145.
 Rourke, M. D., and Ernestine, A. C. (1930). *J. clin. Invest.*, 8, 545.
 Terry, R. (1950). *British Medical Journal*, 2, 1296.
 Westergren, A. (1924). *Ergebn. inn. Med. Kinderheilk.*, 26, 577.
 Wintrobe, M. M., and Landsberg, J. W. (1935). *Amer. J. med. Sci.*, 189, 102.

CORTISONE IN IDIOPATHIC STEATORRHOEA

BY

J. BADENOCH, B.M., M.R.C.P.

(From the Nuffield Department of Clinical Medicine,
Radcliffe Infirmary, Oxford)

Taylor, Comfort, Wollaeger, and Power (1951) have reported favourable results in the treatment of idiopathic steatorrhoea with cortisone in doses of 25–100 mg. daily. Following the administration of the drug, there was subjective improvement, with increased appetite, a rise in the level of plasma proteins and prothrombin, and a significant decrease in the amount of fat and nitrogen excreted in the faeces. There is little evidence of impaired adrenal function in the sprue syndrome, but it is well known that cortisone in this dosage may not be acting as adrenal replacement therapy, and that improvement may occur in a number of conditions in the absence of adrenal insufficiency. We therefore decided to attempt to confirm the results of the Mayo Clinic group.

Remissions are common in idiopathic steatorrhoea, and only patients in whom the clinical condition appeared stable were chosen for trial with cortisone. We selected two untreated patients who had been under observation in hospital, and two others in whom considerable improvement had already occurred after a prolonged period of treatment with diet and vitamins, including folic acid. We felt that if the cortisone had any specific effect on the metabolic defect in steatorrhoea it should produce further improvement in the treated cases and perhaps abolish the steatorrhoea. With established methods of treatment the absorption of fat remains impaired in the great majority of patients.

Method

Each patient was given a diet containing 70 g. of protein and 70 g. of fat daily. The total amount of fat excreted in the stools during three consecutive periods of four days,

separated by carmine markers, was estimated by the method of van de Kamer, ten Bokkel Huinink, and Weyers (1949). One patient who had also been the subject of a calcium balance had a control period of 36 days. At the end of the control period each patient was given 100 mg. of cortisone daily by intramuscular injection for 24 to 28 days, followed by a smaller dose for two to three days before the drug was discontinued.

During the last two weeks of treatment with cortisone a second fat balance was carried out, and the results were compared with those obtained during the control period. In each case the excretion of nitrogen in the faeces was estimated during the period of control, and again during the second fat balance while the patient was receiving cortisone. A radiograph of the chest was taken before treatment was started, and changes in weight, blood pressure, and serum electrolytes were recorded during the trial. Three of the patients, Nos. 1, 2, and 3, were allowed to go home between the two balances, but all were admitted to hospital during the periods of collection of faeces.

Results

Both the patients who had had previous treatment felt better, and in one the bowels were opened less frequently and the stools became more formed. In one of the untreated cases (No. 4) there was a great improvement in appetite and morale, although little change occurred in the action of the bowels. In the other (No. 3) there was no subjective improvement, but the diarrhoea decreased. One patient (No. 2) gained 2.4 kg. in weight during the period of treatment, owing to the retention of fluid.

Excretion of Fat and Nitrogen.—The Chart shows the percentage of dietary fat excreted in the faeces and the amount of faecal nitrogen in each period of four days, before and during treatment with cortisone. The great variation in the results of consecutive estimations in Case 4 was due to irregular bowel action, which made separation of the periods difficult. The Table gives the difference between

Excretion of Fat and Nitrogen in the Faeces Before and During Treatment with Cortisone

Case No.	Mean % Dietary Fat Excreted During Consecutive Periods of 4 Days. (Number of Periods in Parentheses)		Mean 4-day Excretion of Nitrogen in Faeces (g.)		Length of Treatment (Days)	Total Dosage of Cortisone (g.)	
	Before Treatment With Cortisone	During Treatment With Cortisone	Before Treatment With Cortisone	During Treatment With Cortisone			
Previously Treated	1	16.7 (3)	12.0 (3)	7.4	5.2	28	2.80
	2	16.5 (3)	11.1 (3)	6.9	6.9	33	2.88
Previously Untreated	3	43.6 (3)	29.5 (2)	11.1	11.9	31	2.85
	4	25.0 (9)	23.0 (3)	5.6	9.9	28	2.55

For fat excretion: $t = 2.49$; $p > 0.05$.

the mean four-day excretion of dietary fat before and during treatment with cortisone. The difference between the amounts of fat excreted is not significant. The effect on the excretion of nitrogen was variable.

Discussion

Hypotension, pigmentation of the skin, and asthenia are common in patients suffering from steatorrhoea, and several observers, noting the close resemblance to Addison's disease, have suggested that adrenal insufficiency may play some part in the pathogenesis of the sprue syndrome (Gloor, 1930; Thaysen, 1932). However, in spite of the fact that the hormones of the adrenal cortex exert an influence on the

normal process of fat absorption (Bavetta, Hallman, Deuel, and Greeley, 1941; Frazer, 1946), and that an excessive quantity of fat is present in the faeces of some patients with Addison's disease (Bergner, Lewis, Stout, Thorn, and Emerson, 1948), the evidence of adrenal insufficiency in sprue or idiopathic steatorrhoea is slight. Black (1946) showed that the hypotension and asthenia in sprue was not accompanied by an increase in serum potassium or a failure of the kidney to conserve sodium, as might be expected in adrenal failure, and cases of steatorrhoea have been treated with deoxycortone (Leishman, 1945) and corticotrophin (Frazer, 1949) without improvement.

The response to cortisone was not striking, which is in keeping with the belief that adrenal cortical function is normal in cases of steatorrhoea. Each patient improved, but results based on the mean four-day excretion of fat can be quite variable and must be interpreted with caution (Fourman, Higgins, Quelch, O'Brien, and Witts, 1948). Taylor, Comfort, Wollaeger, and Power (1951) found more improvement, but the difference may depend on the selection of patients. In patients suffering from intractable diarrhoea cortisone might prove of greater benefit, for Almy (1951) has reported a severe case in which the diarrhoea and hypoproteinaemia responded to treatment with adrenocorticotrophic hormone when other forms of treatment had failed.

Summary

Four patients with idiopathic steatorrhoea, two of them previously untreated, were given 100 mg. of cortisone daily by intramuscular injection for four weeks.

Although the excretion of fat decreased in all, the difference was not statistically significant, and in none was the steatorrhoea abolished.

I wish to thank Miss Moira Aitken and Miss Beryl Brinkhurst for their assistance in the biochemical investigation, Dr. A. M. Cooke for permission to include one patient who was admitted

under his care, and Professor L. J. Witts for his advice and criticism at all times. I am grateful for the kindness of Dr. Wollaeger and his colleagues, who made their results known to us prior to publication.

REFERENCES

- Almy, T. P. (1951). *Ann. intern. Med.*, **34**, 1041.
- Bavetta, L., Hallman, L., Deuel, H. J., and Greeley, P. O. (1941). *Amer. J. Physiol.*, **134**, 619.
- Bergner, G. E., Lewis, R. A., Stout, F. W., Thorn, G. W., and Emerson, K. (1948). *J. clin. Endocrinol.*, **8**, 606.
- Black, D. A. K. (1946). *Lancet*, **2**, 671.
- Fourman, L. P. R., Higgins, G., Quelch, P., O'Brien, J. R. P., and Witts, L. J. (1948). *Clin. Sci.*, **7**, 121.
- Frazer, A. C. (1946). *Physiol. Rev.*, **26**, 103.
- (1949). *British Medical Journal*, **2**, 769.
- Gloor, H. U. (1930). *Folia Haemat., Lpz.*, **39**, 373.
- Kamer, J. H. van de, ten Bokkel Huinink, H., and Weyers, H. A. (1949). *J. biol. Chem.*, **177**, 347.
- Leishman, A. W. D. (1945). *Lancet*, **2**, 813.
- Taylor, A. B., Comfort, M. W., Wollaeger, E. E., and Power, M. H. (1951). *J. clin. Invest.*, **30**, 678.
- Thaysen, Th. E. H. (1932). *Non-tropical Sprue*, p. 64, Oxford Univ. Press, London.

A recent letter in *Country Life* has the title "Causes of Death in 1711," and gives an account of how a list of old christenings and burials, with causes of death, was found pasted inside the door of a William and Mary marquetry long-case clock. The list refers to London only, and is taken from the reports of the various parish clerks. It covers the year December 12, 1710, to December 11, 1711, during which it records 14,706 christenings and 18,874 burials. Some of the diagnoses of deaths are probably fairly reliable—for example, smallpox 915, death in child-bed 195, and perhaps "stoppage in the stomach 255," rickets 196, and "jandies" (jaundice) 51. But "cancer" is given as only 75, and presumably means externally visible tumours, whether malignant or not, while "rheumatism" numbers 9 and scurvy 2, and the label in these cases is obscure and probably misleading. Some of the causes of death sound very odd to the modern ear. Such are Grief (9), Gripping in the Guts (614), Lethargy (7), Melancholy (1), Surfeit (61), and Teeth (1,013).