Therefore the procainamide was withdrawn and replaced by propranolol 20 mg. q.i.d. The effect was dramatic. The myalgia and arthralgia subsided; the chest symptoms and signs abated, and x-ray examination showed a clear right lung field within one month, followed by a gradual resolution of the effusion on the left side; the E.S.R. fell to 10 mm. in the hour in two months; L.E.-cell preparations were negative after six weeks, and the antinuclear factor was negative five months later.

When seen in October 1966 the patient was well, and was able to do light housework and take mild exercise.

COMMENT

In the 14 cases reported previously, in which similar reactions occurred, procainamide was given in a dosage of 1-5 g. daily. Symptoms of the lupus syndrome appeared after three weeks to 22 months of therapy. The commonest manifestations were polyarthralgia (14 cases), positive L.E.-cell preparations (13 cases), pleuropulmonary symptoms (nine cases), and the presence of antinuclear factor (in all five cases examined). Our patient took 2 g. of procainamide daily for five months before the appearance of chest symptoms.

Apart from two cases that were followed for only seven or eight weeks after procainamide was stopped, all have shown complete recovery within two years. This may represent a difference from the similar syndrome precipitated by hydralazine, in which hypergammaglobulinaemia or antinuclear factor antibodies were found five years after discontinuation of the drug and disappearance of symptoms (Alarçon-Segovia *et al.*, 1965). Recrudescence has been found to follow re-exposure to the drug, but it was not attempted in this case.

There is still much controversy surrounding the mechanism giving rise to this drug-induced syndrome. Some authors Alarçon-Segovia *et al.*, 1965; Lee *et al.*, 1966) feel that the drug unmasks a predisposition to develop lupus erythematosus. Studies in patients with the "hydralazine syndrome" have shown that symptoms and signs possibly due to S.L.E. were present before the drug was given. Patients who at one time had developed clear-cut drug-induced S.L.E. have occasionally been observed to have apparently spontaneous recurrence of the disease years later. There is, however, as yet no case reported

of spontaneous recurrence or chronic S.L.E. induced by procainamide.

There are two other possibilities. Firstly, the symptoms could be a manifestation of drug toxicity or hypersensitivity—that is, a lupus-drug reaction. In favour of this a case has been reported (Prockop, 1966) of a patient with established S.L.E. who received full doses of procainamide for 15 months for a myotonic illness with no exacerbations of S.L.E., though there were episodic symptoms long before and long after the period of drug administration. This may be evidence that the lupus-like drug reaction differs from the disease. Secondly, the appearance of S.L.E. during drug administration might be coincidental, but the increasing number of cases reported makes this unlikely.

A review of the cases would suggest that procainamide is used in circumstances—for example, atrial fibrillation, paroxysmal atrial tachycardia, ventricular ectopics—in America where other drugs would be the first choice in Britain. It was only because this patient, with recurrent ventricular tachycardia, was hypersensitive to quinidine that procainamide was used. It would seem that this drug should be prescribed on a long-term basis only when there is no less potentially harmful alternative.

We wish to express our thanks to Professor O. L. Wade for permission to publish this case, and for advice on the manuscript.

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REFERENCES

- Alarçon-Segovia, D., Worthington, J. W., Ward, L. E., and Wakin, K. G. (1965). *New Engl. J. Med.*, **272**, 462.
Carabia, A. G., and Fortney, T. G. (1965). *J. Tenn. med. Ass.*, **58**, 287.
Colman, R. W., and Sturgill, B. C. (1965). *Arch. intern. Med.*, **115**, 214.
Hahn, A. L. (1964). *Missouri Med.*, **61**, 19.
Kaplan, J. M., Wachtel, H. L., Czarnecki, S. W., and Sampson, J. J. (1965). *J. Amer. med. Ass.*, **192**, 444.
Ladd, A. T. (1962). *New Engl. J. Med.*, **267**, 1357.
Lee, S. L., Rivero, I., and Siegel, M. (1966). *Arch. intern. Med.*, **117**, 620.
Paine, R. (1965). *J. Amer. med. Ass.*, **194**, 23.
Prockop, L. D. (1966). *Arch. Neurol. (Chic.)*, **14**, 326.

Hypoparathyroidism and Malabsorption

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The association of secondary hyperparathyroidism with osteomalacia caused by malabsorption has often been noted (Davies *et al.*, 1956). There also seems to be a connexion between hypoparathyroidism and the malabsorption syndrome.

Bennett *et al.* (1932), in describing 15 cases of "idiopathic steatorrhoea," suggested that five may have had secondary hypoparathyroidism, in view of the finding of a raised serum inorganic phosphorus level. Several cases of idiopathic hypoparathyroidism associated with malabsorption and generalized moniliasis have been described (Collins-Williams, 1950; Salvesen and Bøe, 1953a; Clarkson *et al.*, 1960). A few other cases of idiopathic hypoparathyroidism coexisting with malabsorption alone have been documented in recent years (Lowe *et al.*, 1950; Case Records of Massachusetts General Hospital, 1954; MacGregor and Whitehead, 1954; Jackson *et al.*, 1956; Williams and Wood, 1959; Cochrane *et al.*, 1960; Taybi and Keele, 1962). In a case reported by Clarkson *et al.* (1960) a flat small-bowel mucosa was found on biopsy, and correction of

the hypoparathyroid state converted to normal most of the demonstrated abnormalities of absorption.

CASE REPORT

An unmarried woman aged 58 was admitted to hospital for investigation of an iron-deficiency anaemia which had been present for nine months and had failed to respond to treatment. She gave a history of a "nervous breakdown" followed by depression at the age of 22. A year later she had noticed a progressive deterioration of vision, and was found to have bilateral cataract, one of which was successfully removed at operation.

Clinical examination revealed a pale, nervous woman, with finger-clubbing. A postmature cataract was present in the left eye. Neurological examination showed a positive Trousseau's sign, but a negative Chvostek's sign.

Investigations showed a serum calcium level of 5.7 mg./100 ml. and a serum inorganic phosphorus of 6.1 mg./100 ml. Alkaline phosphatase was within the normal range. The serum albumin and serum iron were low, but serum vitamin B₁₂, folic acid, and cholesterol were normal. Tests for faecal occult blood were consistently negative. Faecal fat collection showed a level of 15 g./day, but D-xylose excretion test gave an equivocal result. Radiology showed no bony change, and small-bowel meal and barium enema

were normal. Electrocardiogram was also normal. Biopsy of the small-bowel mucosa by the peroral method, using the Crosby capsule (Crosby and Kugler, 1957), showed marked villous atrophy with inflammatory changes and epithelial degeneration. The phosphate excretion index (Nordin, 1962; Nordin and Smith, 1965) gave results consistent with hypoparathyroidism.

The patient was treated with calcium supplements and vitamin D₂. After three months the biochemistry was normal, and repeat biopsy of small-bowel mucosa showed minimal damage and a marked improvement from the previous appearances.

DISCUSSION

Hypoparathyroidism and malabsorption have been reported together in more cases than would reasonably be expected by chance. Jackson (1957) thought that the association was well enough documented to be regarded as a "syndrome." There is, however, a lack of uniformity in the principal features of the reported cases. In some the symptoms of malabsorption are dominant, and in others the features of hypoparathyroidism. In most cases the symptoms give no clear indication of the primary condition.

Several possible explanations for the association have been postulated. Salvesen and Bøe (1953b) suggested that intestinal moniliasis may have been the cause in their case, and perhaps in others. This seems unlikely to account for more than a few instances. They also suggest that patients with malabsorption have a relative parathyroid insufficiency due to malabsorption of a substance necessary for the continuation of normal parathyroid activity. There is, however, no evidence favouring the existence of such a substance. Hypocalcaemia may occur with either hypoparathyroidism or malabsorption. The serum inorganic phosphorus is raised in the former, and normal or low in the latter, the depression being caused by compensatory overactivity of the parathyroid gland. There is no evidence that this overactivity will eventually lead to hypofunction of the gland, or any definite evidence that hypoparathyroidism causes intestinal dysfunction and malabsorption. In the present case, if malabsorption were the primary disorder, the serum inorganic phosphorus would be expected to be low, or within the normal range; this would be so if the patient was responding normally to the low serum calcium level due to poor absorption. In fact, however, the level is high, as in most of the cases reported. This suggests that the hypoparathyroidism may be the primary abnormality in many of the reported cases.

In the present case there is abundant evidence favouring a long-standing hypoparathyroidism. The development of bilateral cataract so early in life, together with mental symptoms (Clark *et al.*, 1962; Denko and Kaelbling, 1962), suggests that the condition was present 35 years ago. It is also known that hypoparathyroidism, whatever the cause, may remain latent for many years (Bull and Dillihunt, 1965). It seems likely that this patient's malabsorption was not of very long standing, as the symptoms of anaemia and possibly other deficiencies would have occasioned her attendance at hospital earlier. In addition, the treatment given in an attempt to improve parathyroid function resulted in an improvement in absorptive capacity of the small bowel, together with considerable restoration towards normal of the mucosal appearances. For these reasons, and the high serum phosphorus level, there is a possibility that parathyroid hypofunction has caused damage to the mucosa of the small bowel. None of the cases reported in the literature are incompatible with this hypothesis. This patient may therefore fall into the secondary coeliac syndrome group postulated by Hindle and Creamer (1965a, 1965b). They found that 36% of patients with a flat jejunal mucosa had some associated disease in addition to the symptoms of malabsorption. The

primary disease may have been present for many years before malabsorption developed. They found it impossible to differentiate between primary and secondary coeliac syndrome groups on the basis of the deficiencies present and in the response to treatment. In some cases the mucosal changes were reversible with treatment of the underlying disease.

A wide list of conditions have been described as being associated with malabsorption and a flat jejunal mucosa. These include carcinoma (Creamer, 1964), malignant lymphoma (Gough *et al.*, 1962), diabetes mellitus (Mailman, 1958; Ellenberg and Bookman, 1960; Vinnik *et al.*, 1962), ulcerative colitis (Goulston, 1964; Salem *et al.*, 1964), infectious hepatitis (Astaldi *et al.*, 1964), tuberculosis and sarcoidosis (Hindle and Creamer, 1965a, 1965b), hepatic cirrhosis (Salem *et al.*, 1964), uraemia and congestive cardiac failure (Lochry and Creamer, 1966), and the dermatoses (*Lancet*, 1965). Hypoparathyroidism may therefore be regarded as one more disease which can cause the secondary coeliac syndrome.

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REFERENCES

- Astaldi, G., Grandini, U., Poggi, C., and Strosselli, E. (1964). *Amer. J. dig. Dis.*, **9**, 237.
Bennett, T. I., Hunter, D., and Vaughan, J. M. (1932). *Quart. J. Med.*, **25**, 603.
Bull, D. M., and Dillihunt, R. C. (1965). *J. Amer. med. Ass.*, **193**, 308.
Case Records of Massachusetts General Hospital (1954). *New Engl. J. Med.*, **251**, 442.
Clark, J. A., Davidson, L. J., and Ferguson, H. C. (1962). *J. ment. Sci.*, **108**, 811.
Clarkson, B., Kowlessar, O. D., Horwith, M., and Sleisenger, M. H. (1960). *Metabolism*, **9**, 1093.
Cochrane, W. A., Morse, W. I., and Landrigan, P. (1960). *Amer. J. Dis. Child.*, **100**, 544.
Collins-Williams, C. (1950). *Pediatrics*, **5**, 998.
Creamer, B. (1964). *Brit. med. J.*, **2**, 1435.
Crosby, W. H., and Kugler, H. W. (1957). *Amer. J. dig. Dis.*, **2**, 236.
Davies, C. R., Dent, C. E., and Willcox, A. (1956). *Brit. med. J.*, **2**, 1133.
Denko, J. D., and Kaelbling, R. (1962). *Acta psychiat. scand.*, **38**, Suppl. No. 164.
Ellenberg, M., and Bookman, J. J. (1960). *Diabetes*, **9**, 14.
Gough, K. R., Read, A. E., and Naish, J. M. (1962). *Gut*, **3**, 232.
Goulston, K. J. (1964). *Ibid.*, **5**, 490.
Hindle, W., and Creamer, B. (1965a). *Brit. med. J.*, **2**, 455.
— (1965b). *Ibid.*, **2**, 458.
Jackson, W. P. U. (1957). *Lancet*, **1**, 1086.
— Hoffenberg, R., Linder, G. C., and Irwin, L. (1956). *J. clin. Endocr.*, **16**, 1043.
Lancet, 1965, **2**, 69.
Lochry, C. A., and Creamer, B. (1966). *Brit. med. J.*, **1**, 827.
Lowe, C. U., Ellinger, A. J., Wright, W. S., and Stauffer, H. M. (1950). *J. Pediat.*, **36**, 1.
MacGregor, M. E., and Whitehead, T. P. (1954). *Arch. Dis. Childh.*, **29**, 398.
Mailman, R. H. (1958). *Ann. intern. Med.*, **49**, 190.
Nordin, B. E. C. (1962). *Scot. med. J.*, **7**, 74.
— and Smith, D. A. (1965). *Diagnostic Procedures in Disorders of Calcium Metabolism*. London.
Salem, S. N., Truelove, S. C., and Richards, W. C. D. (1964). *Brit. med. J.*, **1**, 394.
Salvesen, H. A., and Bøe, J. (1953a). *Acta med. scand.*, **146**, 290.
— (1953b). *Acta endocr. (Kbh.)*, **14**, 214.
Taybi, H., and Keele, D. (1962). *Amer. J. Roentgenol.*, **88**, 432.
Vinnik, I. E., Kern, F., and Struthers, J. E. (1962). *Gastroenterology*, **43**, 507.
Williams, E., and Wood, C. (1959). *Arch. Dis. Childh.*, **34**, 302.